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APPRECIATION OF DR. RICHARD M. PEARCE.

THE PATHOLOGICAL POSSIBILITIES OF NEGLECTED GALL-STONE DISEASE. By JOHN B. DEAVER, M.D. 733

SPECULATIONS REGARDING THE NATURE OF CANCER. By A. L. BENEDICT, A.M., M.D. 742

HEART MUSCLE EQUATIONS. By HAROLD W. DANA, M.D. 750

ADVANCEMENT IN THE TREATMENT OF WOUNDS AND INFECTIONS RESULTING FROM THE WAR. By JOHN H. GIBBON, M.D. 764

SOME CLINICAL MANIFESTATIONS OF INFLUENZA IN CHILDREN. By LINNAEUS E. LA FÉTRA, M.D. 770

PRIMARY CARCINOMA OF THE VERMIFORM APPENDIX: A REVIEW OF THE LITERATURE, WITH A REPORT OF TWO NEW CASES. By EDWARD E. H. BOYER, B.Sc., M.Sc. 775

HUMAN ANTHRAX. By JOSEPH C. REGAN, M.D., and CATHERINE REGAN, M.D. 782

THE METHOD OF OBTAINING CEREBROSPINAL FLUID BY PUNCTURE OF THE CISTERNA MAGNA (CISTERN PUNCTURE). By PAUL WEGEFORTH, Captain, M.C., U.S.A., JAMES B. AYER, Captain, M.C., U.S.A., and CHARLES R. ESSICK, Captain, M.C., U.S.A. 789

ACUTE HEMATOGENOUS STREPTOCOCCIC PERITONITIS. By MEYER A. RABINOWITZ, M.D. 797

PATHOLOGY OF (MUSTARD?) GAS INHALATION. By GEORGE W. COVEY, M.D., M.C., U.S.A., and MOSES BARRON, M.D., M.C., U.S.A. 808

CLIMACTERIC HYPERTENSION: A STUDY OF HIGH BLOOD-PRESSURE DURING AND FOLLOWING THE MENOPAUSE. By ARTHUR H. HOPKINS, M.D. 826

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CONTENTS

ORIGINAL ARTICLES

Appreciation of Dr. Richard M. Pearce

The Pathological Possibilities of Neglected Gall-stone Disease . . . 733
By JOHN B. DEAVER, M.D., Philadelphia, Pa.

Speculations Regarding the Nature of Cancer 742
By A. L. BENEDICT, A.M., M.D., Consultant in Digestive Diseases, Columbus Hospital; Attendant, Mercy Hospital, Buffalo.

Heart Muscle Equations 750
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Advancement in the Treatment of Wounds and Infections Resulting from the War 764
By JOHN H. GIBBON, M.D. (late Colonel, M.C., and Consultant in Surgery, A. E. F.), Philadelphia, Pa.

Some Clinical Manifestations of Influenza in Children 770
By LINNAEUS E. LA FÉTRA, M.D., Associate in Pediatrics, Columbia University; Director of the Children's Medical Service, Bellevue Hospital, New York.

Primary Carcinoma of the Vermiform Appendix: A Review of the Literature, with a Report of Two New Cases 775
By EDWARD E. H. BOYER, B.Sc., M.Sc., Columbus, Ohio.

Human Anthrax 782
By JOSEPH C. REGAN, M.D., Resident Physician, and CATHERINE REGAN, M.D., Resident Pathologist; Kingston Avenue Contagious Disease Hospital, New York City.

(Contents continued on page 8)

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Acute Hematogenous Streptococcic Peritonitis 797

By MEYER A. RABINOWITZ, M.D., Associate Physician to the Greenpoint Hospital; Assistant Physician and Assistant Neurologist to the Jewish Hospital, Brooklyn, N. Y.

Pathology of (Mustard?) Gas Inhalation 808

By GEORGE W. COVEY, M.D., M.C., U.S.A., Lincoln, Nebraska, and MOSES BARRON, M.D., M.C., U.S.A., St. Paul, Minnesota.

Climacteric Hypertension: A Study of High Blood-pressure During and Following the Menopause 826

By ARTHUR H. HOPKINS, M.D., Instructor in Medicine and in Practical Therapeutics in the University of Pennsylvania; Assistant Physician to the University Hospital.

REVIEWS

Surgery of the Spine and Spinal Cord. By Charles H. Frazier, M.D. . 837

Diseases of the Heart and Bloodvessels. By Thomas E. Satterthwaite, A.B., M.D., LL.D., ScD. 838

Physical and Occupational Reëducation of the Maimed. By Jean Camus 839

Quarterly Medical Clinics. By Frank Smithies, M.D. 840

The Humane Society of the Commonwealth of Massachusetts: An Historical Review, 1785–1916. By M. H. De Wolfe Howe 840

Gilbertus Anglicus Medicine of the Thirteenth Century. By Henry E. Handerson, A.M., M.D. 841

War Surgery from Firing Line to Base. By Basil Hughes, Temporary Major, R.A.M.C., T.F., and H. Stanley Banks, Captain, R.A.M.C., T.C. 841

The Action of Muscles, Including Muscle Rest and Muscle Reëducation. By William Colin Mackenzie 842

The Organs of Internal Secretion. By Ivo Geikie Cobb, M.D., M.R.C.S. 843

An Introduction to the Mammalian Dentition. By T. Wingate Todd . 844

Annual Report of the Department of Pathology of the Johns Hopkins University and Hospital 844

(*Contents continued on page 10*)

CLINICAL LABORATORY ANALYSES

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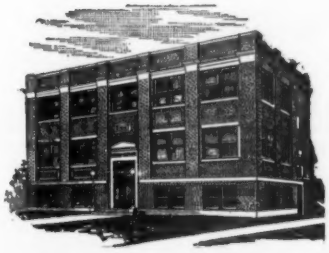

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Treatment of Ununited Gunshot Fractures 845
Changes in Growing Bone after Injury to Epiphyseal Cartilage Plate . 846
Study of Buried Bone 847
Abduction Treatment of Fracture of the Neck of the Femur 847
Shall Operation for Hypertrophied Prostate Be Done in Two Stages? . . 848
Carcinoma of the Stomach 848

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Treatment of Influenza 849
Fatigue in Irritable Heart and Other Conditions 850

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Influenza Occurring in Pregnant Women 851
Influenza in the Newly Born Infant 852
Placental Tissue as a Galactagogue 853
Rotation of the Head by Forceps in the Occipitoposterior Position . . 853

(*Contents continued on page 12*)

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Cure of Prolapse in the Aged 855
Radium in Cancer 855
Operative Results in Myoma Uteri 856
Lacerations of the Vagina from Coitus 857
Polypoid Adenoma of the Uterus 858

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.

Determination of the Length of Life of Transfused Blood Corpuscles in Man 859
Observations on the Wassermann Reaction 859
Pathology of Epidemic Influenza 860
How the United States is Meeting the Tuberculosis War Problem . . 861
Regulation of the Intestinal Flora of Dogs through Diet 862
Perfusion Experiments in the Study of Cellular Anaphylaxis 863

(*Contents continued on page 14*)

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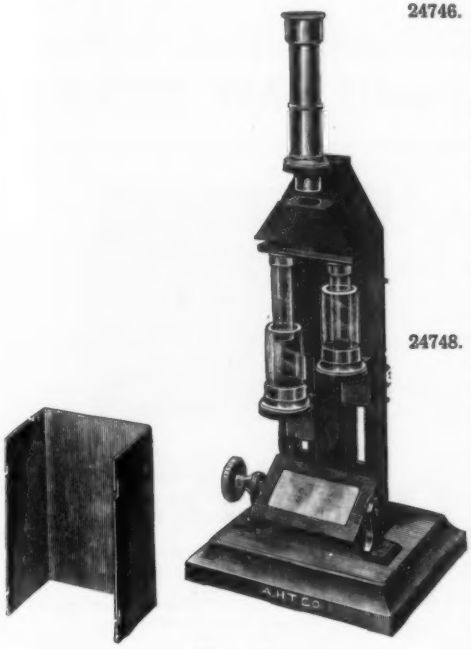

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CONTENTS—(*Continued*)

HYGIENE AND PUBLIC HEALTH

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MILTON J. ROSENAU, M.D., AND GEORGE W. McCOY, M.D.,

Effective Malaria Control in a Rice-field District 864
Persistence of the Virus of Poliomyelitis in the Nasopharynx 864
The Role of the Hand in the Distribution of Influenza Virus and the Secondary Invaders 865
The Effect of Heat, Age and Reaction on the Antiscorbutic Potency of Vegetables 866

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*United States Public Health Bulletin No. 69, May, 1915.

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DR. RICHARD M. PEARCE

AN APPRECIATION OF DR. RICHARD M. PEARCE.

With the strain and turmoil of the war behind us, we are beginning to view the stirring and momentous events of the past two years in proper perspective. To the thoughtful it becomes increasingly apparent that victory was not alone the result of valor on the battle-fields of France. Without the widespread coöperation and thorough organization of all industries and activities in this country, the never-to-be-forgotten exploits and accomplishments of our Armies could not have been carried out. The rapid mobilization and successful direction of our vast and varied resources were made possible through the unselfishness of those leaders in all branches of work who so willingly and freely gave of their services and experience. Among this group must be numbered the many members of the medical profession who, in spite of their disappointment at being denied active service in the Army overseas, faithfully and loyally performed countless duties at home, duties which, though less dramatic and spectacular, were, nevertheless, no less arduous and exacting than those that had to be accomplished in the Army abroad. Of this coterie of patriotic physicians, none is more justly deserving of credit and distinction than Dr. Richard Mills Pearce, lately Major, Medical Corps, United States Army.

It is not our purpose here to recount his notable achievements as Chairman of the Division of Medicine and Related Sciences of the Council of National Defence, nor to dwell upon his invaluable aid to the Army when, after accepting a commission, he became closely identified with the work and organization of the Laboratory Section of the Army Medical Department. His successes along these lines are already a matter of record and are too widely known to require further comment. It is our desire, however, to give to Dr. Pearce some measure of the recognition and credit he deserves for having assumed voluntarily, in addition to his other many duties, the task of editing the American Journal of the Medical Sciences while its regular Editors were absent in the military service.

Early in the summer of 1917 he undertook this work, and from then until last February he carried it on, in spite of the ever-increas-

ing burdens that were heaped upon him. The readers of this JOURNAL can amply testify to the success that attended his editorial supervision. Not only did he procure an adequate amount of material for publication, but he saw to it that the contributions published, both in scientific value and practical interest, were in keeping with the traditional standards maintained by this publication. All this he did in the face of such unprecedented difficulties as the unsettled state of the whole medical profession; the absence of many regular contributors in the Army; and the hopelessly overworked condition of those who still remained in the civilian ranks.

Therefore, it is with a sense of deepest gratitude that the returning Editors, as well as the publishers of the JOURNAL, take this opportunity of expressing to Dr. Pearce their heartiest thanks for and sincerest appreciation of what he has so graciously done, not only for them personally and for the JOURNAL, but also for the entire medical profession of America.

Credit is also due Professor A. N. Richards, Dr. O. H. P. Pepper and the others who from time to time assisted Dr. Pearce in this work.

Our thanks are likewise extended to Miss Susanna Stern, who throughout the duration of the War ably saw every issue through the press.

The Editors freely acknowledge their debt to Dr. Pearce, and fully realize that only through the personal interest and zeal displayed by him, and also by those who assisted him in his work, has it been possible for the oldest medical monthly in the United States, the one that survived the turbulent days of our own Civil War, to continue its uninterrupted existence during the world-wide struggle that has just terminated and to withstand so successfully the vicissitudes of the past two years.

G. M. PIERSOL.

THE

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OF THE MEDICAL SCIENCES

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ORIGINAL ARTICLES

THE PATHOLOGICAL POSSIBILITIES OF NEGLECTED GALL-STONE DISEASE.[1]

By John B. Deaver, M.D.,

PHILADELPHIA, PA.

The benefits of exchanging experience and discussing impressions that come to the worker in every field of endeavor are probably nowhere more apparent than in the domain of medicine and surgery; witness the numerous medical societies and associations that abound in all sections of the country, great and small, meeting at stated times to coördinate and correlate the observations that have come to their members each in his own field. It is this interpretation that I have put upon your cordial invitation to appear before you this evening, and with this idea in mind I have chosen for my subject the consequences of neglected gall-stone disease, the baneful effects of which must be apparent to every surgeon doing a large amount of work in the upper right abdomen. It is perhaps only the far-reaching effects of trifling with disease of the appendix that can compare with the consequences of allowing gall-stone disease to progress beyond certain definite limits, *i. e.*, a second attack of cholecystitis.

The varieties of gall-stone disease that most commonly lead to complications and sequels that so often are the bugbear of the surgeon, and the cause of untold suffering to the patient, to say nothing of chronic invalidism, and, in some instances, death, are chole-

[1] Read before the Medical Association of the Greater City of New York, April 21, 1919.

cystitis, stone in the common duct (with or without jaundice), cholangitis, pancreatic lymphangitis, chronic pancreatitis and carcinoma of the gall-bladder; for inasmuch as the three last-named are the direct result of neglected gall-stone disease, they are legitimately to be considered as varieties of that disorder.

The chief agent in the drama that often develops into such an unfortunate tragedy is cholecystic inflammation, resulting in pericholecystic adhesions, infection of the liver and the pancreas. This does not refer to the adhesions that form in ordinary pericholecystic inflammation but to the dense adhesions that are encountered in the shape of a peritoneal sheet practically enveloping the pylorus and the duodenum—in other words, pathological peritoneum, the term I use in describing the condition to my students. In addition to this enveloping membrane there are often strong bands that bind the pylorus, the duodenum, the hepatic flexure of the colon and the great omentum, and in some instances the tip of the appendix to the gall-bladder and the liver, so as to make recognition of the individual organs almost impossible. To separate this vicious conglomerate mass in certain cases would necessitate adding at least a crowbar, hatchet and trowel to the armamentarium of the operating room. This is no exaggeration; for too often it would be a serious matter even to attempt to separate such entangling alliances without running the risk of traumatic injury; gall-bladder, duodenal or gastric fistula being among the evils, and probably the mildest ones that might be expected to follow.

It goes without saying that this pathological sheet is not to be confounded with congenital peritoneal abnormalities. If I may be permitted to digress for a moment, I should like here to say that I have not met with the embryonic bands, veils and sheets of peritoneum so frequently mentioned in the literature as causative factors in intestinal stasis. I have always believed, and still believe, that they are the result of pathology, and as such only deserve serious consideration.

But these adhesions are not alone due to inflammation of the gall-bladder. In a percentage of cases they may be caused by an ulcer of the duodenum or an ulcer abutting on the pylorus that has invaded all the coats of the duodenum. This is often seen in subacute perforation of several days' standing. But whether the duodenum in the shape of ulcer is the seat of the pathology, or whether it is the infected gall-bladder, cannot always be determined until the peritoneal sheet, above referred to, is lifted. This, however, may sometimes be a dangerous proceeding, and it takes the experienced eye to judge at a glance of the wisdom of occasionally doing nothing more than performing a posterior gastro-enterostomy. It is obvious, therefore, that an effective method of preventing this aspect of the pathology of gall-bladder disease is the early surgical treatment of cholecystitis. It is an erroneous notion, all too preva-

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lent even at this day, that gall-bladder disease is a surgical condition only when it has actually become gall-stone disease. Gall-stones are but one of the sequels, and, as we have seen, not one of the most important sequels of cholecystic inflammation. At the same time it should be remembered that "gall-stones are foreign bodies which need only infection to lead to the most widespread cholangitis, biliary cirrhosis and pancreatitis."

Cholecystitis is among the most frequent infections within the upper abdomen, and is also one of the most common causes of chronic indigestion. It is rarely diagnosed before middle life, because it is generally considered a disease peculiar to that period. In early life the symptoms are liable to be unobtrusive and escape recognition, but that it does occur in the twenties and thirties, and even earlier, is evidenced by the histories of our gall-stone cases and by the well-known tenacious persistence of cholecystic infection, as illustrated in typhoid cholecystitis. It is a generally accepted fact that a gall-bladder once infected rarely, if ever, resumes its normal aspect. Even after so-called cures, infection is probably always more or less active until it is removed by cholecystectomy or until it converts the gall-bladder into an atrophic functionless mass. In either case the function of the gall-bladder is dispensed with, in the second instance there is the continuous menace of degenerative reaction, while in the other the prospect is for regenerative phenomena.

To the experienced surgeon operations on the biliary passages ordinarily present few difficulties, but when confronted with the pathology I am referring to he is often staggered. Owing to the long-continued disturbance in the bladder, stone or stones at first, if wandering, may have been floated out with the bile. But later on, when they become dislodged by contraction of the gall-bladder, owing to inflammatory irritation of the bile as the result of renewed infection, they may lodge in the cystic duct, but they most commonly lodge in the common duct, occasionally in the hepatic duct, with damming up of the bile, leading to changes in the gall-bladder, liver, the intestines, etc. The gall-bladder demanding an outlet for the bile may force an opening into the duodenum. The whole area becomes masked by adhesions binding the various viscera to each other in bonds stronger than any that can be devised at the Peace Conference to hold the nations together in an amicable league. The ideal procedure, when encountering such an appalling condition, would be to remove the obstruction of the common duct and allow nature's artificial anastomosis, if I may be allowed the contradiction of terms, to remain. But the landmarks may have become so destroyed that it is impossible to locate the common duct and to provide against accidents which may happen through possible abnormalities in the regional anatomy. The gall-bladder cannot be removed *in toto* because of its close adherence to the duodenum.

How then is such a condition to be treated? The decision which will give the patient the best chance must be made quickly, with results that are not always immediately satisfactory. This is well illustrated in the following case:

Mrs. ——, aged sixty-one years, for ten years had suffered with attacks of severe cramp-like epigastric pain radiating to the right shoulder, requiring morphin for relief. The attacks came on after eating, and were followed by vomiting, but never by jaundice. In the interval between attacks she was free from digestive troubles, but complained of weakness and dyspnea. Bowels were regular.

On the day of admission, March 10, 1919, to the Lankenau Hospital, Philadelphia, while shopping, she was seized with one of these attacks, which was ushered in by severe sweating. She reported having had four seizures during the past summer, the last one in August. Examination showed a well-nourished elderly woman. Slight icterus of sclera. Slight pharyngitis, with mucoid expectoration. Heart and lungs negative. Abdomen: rigidity over right side of abdomen with tenderness, most marked over the upper right rectus. Peristalsis present. No masses felt. Pulse of good tension; no sclerosis. Blood-pressure, 140; 80. Gastric analysis showed some hyperacidity.

Roentgen-rays of biliary and genito-urinary tracts were negative.

At operation the following conditions were found: The pylorus and duodenum were adherent to the liver and the gall-bladder. Pylorus separated. The gall-bladder and duodenum were so densely adherent that it was thought best not to attempt to separate them, but instead to make the inspection of the common duct safer by opening the gall-bladder and introducing the finger into it. The point of the finger, as it was carried to the fundus of the gall-bladder, entered the duodenum, showing that nature had made a cholecystoduodenostomy. The posterior wall of the gall-bladder was adherent to the common duct, which was solid with stony material. The gall-bladder was cut across and the two portions, with difficulty, dissected from the common duct—the upper portion with the cystic duct removed and the lower portion invaginated, in this way closing the anastomotic opening. The common duct thus laid bare in its first or supraduodenal portion was opened, and stones and stony debris, with foul-smelling pus removed; the latter in large amount also flowed out of the hepatic duct.

Three days after the operation the patient began discharging gastric contents through the wound and grew progressively weaker. A purse-string suture was placed (by the house surgeon) around a visible fistulous opening. This held for four days, during which time the patient improved considerably, but it broke down again and a second operation was necessary.

At the second operation the duodenum above the original anastomotic opening was partially necrosed, therefore, the only thing

left to do was amputation and inversion of the duodenum below the anastomosis, closure of the pylorus and posterior gastro-enterostomy. Immediate improvement set in, followed by complete recovery.

Stone or stones in the common duct ordinarily are not very serious if operated early. But when impaction of the duct by several stones, or stony material, takes place the state of things is serious and menacing. In such an instance the hepatic duct is also usually involved, resulting in a calculous cholangitis, occasionally with miliary abscess of the liver, that adds materially to the mortality records. The following case is an example:

Mr. ——, aged fifty-five years, gave a history of indigestion for several years, with occasional attacks of severe epigastric pain, followed a number of times by jaundice. While travelling from New York to Washington he was seized with such an attack, which necessitated his interrupting his journey at Philadelphia. When I saw him several days later he was intensely jaundiced and was having two or three chills daily, followed by high temperature and profuse sweats. His liver was enlarged and tender. I advised immediate drainage of the common duct. At operation the duct was found impacted with stones the size of millet seeds, similar ones being also present in the hepatic duct. The ducts were emptied as well as possible and the common duct drained. The patient improved temporarily, but finally succumbed. Autopsy: cholangitis. Thousands of minute stones were present in the small ducts of the liver, with very many small pus foci.

May I ask what medical treatment did for these patients? Answer: Hurried the latter to an untimely grave and jeopardized the life of the former by placing her in the surgeon's hands at a time when it was nearly too late.

Diffuse calculous cholangitis holds the same relation to the liver as does multiple minute abscess formation following upon pylephlebitis, which means that all the patients die, do what you will. Moral, operate before either occurs.

Cholangitis, as evidenced by the foregoing illustrative case, is only one of the sequels of neglected cholecystic disease. The pericholecystic exudates, if allowed to progress to organization, bring with them a train of evils in the way of interference with gastric and duodenal motility, the symptoms of which are treated in various ways, but rarely in the proper way, because the correct diagnosis has not been made. What the tragic consequences may be is seen in the following instance:

Mrs. ——, aged fifty-four years, for the past ten years has been suffering from indigestion, consisting of heaviness, burning sensation, eructations in the epigastrium, coming on from one-half to two hours after meals. On four occasions during this time she had attacks of severe pain in the right upper abdominal quadrant. For

the past two months vomiting spells after meals have been frequent, the last one having occurred a week ago.

Physical examination was negative, except for slight icteric scleræ and tenderness on slight pressure in the gall-bladder region. Blood-pressure, 160; 100.

At operation a mass of adhesions surrounded the gall-bladder to the right, and with the fundus of the gall-bladder, to which they were adherent, formed a hard mass the size of a tennis-ball, with the tip of the appendix adherent. After carefully separating the adherent viscera by dissecting with the knife, scissors and crowbar the gall-bladder, containing stones, was removed. The appendix, its tip containing pus, was also removed. The adherent wall of the duodenum was the site of a pressure ulcer which had gone through the serosa and into but not through the muscularis. This was oversewn.

The pathology that results from delayed intervention for common duct cholelithiasis is serious, indeed, much more serious than that produced by stones elsewhere. The effects are not local but general, from the direct influence on the physiological activities of the hepatic ducts and their radicles, through absorption by the lymphatics along the duct and from the effect on the gastro-intestinal tract by interference with the functions of the pancreas and the intestines.

Stones in the cystic duct, while not so serious, are of sufficient moment to warrant earnest consideration; for although they may cause partial or complete closure of the duct the resulting inflammation may subside and allow the duct to remain patent and permit a return to normal physiology; but the presence of the stone or stones acts as an irritant, and without doubt favors subsequent infection.

The following two cases illustrate what can occur as a result of delayed common duct and cystic duct cholelithiasis:

Mrs. ——, for a number of years the subject of indigestion, which formed the premonitory symptoms of gall-stone disease, finally comes to operation (by another surgeon—a very good one, too) for stone obstruction of the common duct. The numerous adhesions caused great difficulty in locating and exposing the common duct, from which one stone was removed. He suspected that there were more stones, but on account of the condition of the patient and the difficulty he had had in extracting this one stone he introduced drainage into the common duct and closed the wound. The patient improved somewhat, but never got entirely well. Finally, at the suggestion of the original operator and her family physician, she was referred to me and we agreed that reoperation was the only course that promised permanent recovery.

The duodenum, pylorus, common duct, gall-bladder, hepatic flexure of the colon and great omentum were found to be plastered into a conglomerate mass. After much difficulty in exposing the

common duct, and with the unavoidable traumatism that would naturally occur, I succeeded in removing a rather large stone from the duct, which on being probed was then found patulous; a T-tube was introduced into the common duct. The patient recovered from the immediate effects of the operation and went along comparatively well for ten days, when she commenced to vomit at intervals of ten to twenty-four hours. The vomitus showed retention of nourishment taken several hours before. The stomach capacity and the amount of retention were determined and indicated pyloric obstruction. Posterior gastro-enterostomy was then done which was followed by prompt relief. Unfortunately, ten days later regurgitant vomiting ensued, necessitating a third operation, entero-enterostomy, for relief. This patient is now well.

The case of cystic duct cholelithiasis occurred in a young woman who for a number of years had had numerous attacks of gall-stone colic in the winter and had been in the habit of spending the summer in Carlsbad taking the cure; but the attacks always appeared again. She finally came to operation, when there was found a stone impacted in the cystic duct that had formed a union with the pylorus and had ulcerated down to the mucosa. The stone together with the gall-bladder were removed and an ulcerative opening in the pylorus oversewn; this was followed by recovery.

The patient remained well for one year, when trouble indicative of gastric retention appeared. This went on for three years, the patient relieving herself with the stomach tube, used twice daily. She eventually consulted a gentleman in your city, her home-town. Roentgen-ray examination demonstrated pyloric obstruction. It was my privilege to do a gastro-enterostomy and take out a chronically diseased appendix. The patient at the end of two years remains well and enjoys normal health.

The effects on the pancreas are as far-reaching as any of the sequels of neglected gall-stone disease, which we have been discussing, and as disastrous. The route of infection of this organ so closely allied to the gall-bladder, the duodenum and the other abdominal viscera is well known, and the regularity with which the inflammation attacks first the head of the pancreas in the form of pancreatic lymphangitis, the forerunner of chronic pancreatitis, is also a fairly well-established fact.

Pancreatic lymphangitis is nearly always related to gall-bladder inflammation, and is most easily recognized in this connection; but it also can and does result from lymphatic infection from the pylorus and duodenum, the association of duodenal ulcer and pancreatitis being not very uncommon. From personal experience I have observed peripancreatic and pancreatic inflammation traceable to an infected appendix, the route of infection being retroperitoneal and through the lymphatics along the cystic and common ducts. Unfortunately, the lesions of this prepancreatic condition

are comparatively slight and at autopsy are apt to be confused with the autodigestion of the pancreas that takes place after death. But since attention has been called to this condition, and with the present knowledge of the pathology as seen from its effects on the pancreas, which appears at the operating table, the importance of early surgery for any of the primary conditions which have been briefly referred to cannot be overemphasized.

It seems to me to be particularly unfortunate when the effects of trifling with indications of some biliary disturbances lead to the ultimate death of a young woman who has just tasted the joys of motherhood.

Mrs. ——, aged thirty-two years, gave a history of three, if not six, years of gastric disturbance. Six years before her admission to the Lankenau Hospital she had complained of fulness, pain and distention in the epigastric region, followed by vomiting. The condition lasted three or four months, leaving considerable soreness in the right upper abdomen. She experienced no further trouble until three years later, when the symptoms were repeated, but with greater severity. She had since then been suffering with gaseous and acid eructations. In none of these attacks was she jaundiced. About one month before admission to the hospital, five days before the birth of her child, she was seized with sudden pain in the epigastrium, lasting a few minutes, but followed by continual vomiting until she was delivered. Three days later she became deeply jaundiced. The jaundice fluctuated once. Her stools had at times been clay-colored and the urine bile-stained. Bowels extremely constipated.

Physical examination negative except for the deep jaundice and tenderness on pressure in the right hypochondrium. After admission the patient was given castor oil, which she vomited. She then developed severe colicky pains in the right upper abdomen, radiating to the left shoulder. Relief came only after four injections of morphin.

Operation was performed ten days after admission. On opening the peritoneum a greenish-brown fluid escaped. Some fat necrosis was observed on the omentum. The gastro-colic omentum was incised, exposing a necrotic pancreas. Rather free bleeding occurred on blunt dissection of the pancreas, which was controlled by gauze packing. A distended gall-bladder was then exposed and tapped, emitting a greenish bile. Several small stones were removed from the gall-bladder.

Oozing from the wound followed during the postoperative course. Two blood transfusions were performed and calcium and horse serum administered. The wound was opened and packed with dry sterile gauze impregnated with sterile boracic acid, but death ensued on the fifteenth day after operation.

The pancreas, the most important organ of the digestive tract,

is responsible for many cases of upper abdominal distress, which we often hope to correct by removal of the appendix, and the gall-bladder. As we all are well aware, this is not always followed by entire relief of symptoms. The recurrence of symptoms after gall-bladder operations is a favorite topic of discussion among surgeons. On the strength of my experience in these conditions I am of the opinion that it is necessary to go further, and when the condition of the gall-bladder permits in not a few instances, I make it a practice to do cholecystoduodenostomy. The removal of the gall-bladder, the site of interstitial changes, in the presence of enlargement of the glands along the cystic and common ducts, will in some cases fall short of bringing about the desired result. In those cases where, in addition to enlargement of the above-mentioned glands, the glands beyond and more intimately related to the pancreas are enlarged, it is my practice to do an anastomotic operation; this seems to correct the condition and to bring about a restoration to the normal. I have done this again and again, with most gratifying results.

That carcinoma of the gall-bladder may result as a sequel to calculous cholecystitis cannot be denied. Recently, I operated for a condition diagnosed carcinoma of the hepatic flexure of the colon. The patient, a woman, aged seventy years, had been a constant sufferer from upper abdominal discomfort, which had been at various times interpreted as gall-stone disease. When I saw her in consultation the most pronounced symptoms were pain, nausea, marked constipation, exhaustion and weakness after a bowel movement, secured only by purgatives, loss of weight, anemia, later confirmed by the blood picture. Examination revealed the presence of a hard tumor in the upper right abdomen, which was confirmed by the roentgen rays. This, together with the symptoms, suggested carcinoma of the colon. At operation I found a diseased gall-bladder filled with stones, and upon its inner wall, midway between the fundus and the neck, a carcinoma adherent to and infiltrating the great omentum, which in turn was adherent to the serosa of the hepatic flexure of the colon, indenting the bowel so as partly to obstruct its lumen.

I have refrained from touching upon the more remote possibilities of cholecystic infection, such as subdiaphragmatic abscess and subhepatic infection, which often are difficult to deal with. A discussion along these lines would hardly be germane to my subject, except to call attention to their importance in relation to what has gone before.

I shall be satisfied if what I have said proves of value to the surgeon and convinces the physician of the dangers of persistent medical treatment for conditions which, as I hope to have succeeded in demonstrating, surgery alone can relieve. I do not hesitate to maintain that medical treatment is to a great extent responsible for many of the dire results I have portrayed. Somebody is certainly at fault. Who is at fault?

SPECULATIONS REGARDING THE NATURE OF CANCER.

By A. L. Benedict, A.M., M.D.,

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Relation to Acidity. The writer has previously called attention to the fact that about three-fourths of all cancers arise in parts that either have an acid secretion or are prone to acid fermentation. With more or less variation in actual proportions, this can be verified from any statistics. It is partly coincidental, to the extent that a large proportion of epithelium is exposed to acid contact while mesoplastic tissues are never so exposed physiologically and only exceptionally pathologically, but, comparing the epithelium of the alimentary canal, including its offshoots into the liver and pancreas and its less direct embryological extensions, according to reaction, a very great preponderance of cancer is noted in parts subject to acid contact. It is not intended to claim that the actual fact as to preponderance of cancer in acid parts is significant nor has it been possible to test the significance by a therapeutic application of a hypothesis as to the influence of reaction on the growth of cancer.

Essential Identity or Difference of Carcinoma and Sarcoma. Both these diseases and the less common types of malignant new formation, including even leukocythemia, present analogies to infections, and while every germ thus far claimed has been disproved, the same was true of syphilis until quite recently, and yellow fever, scarlet fever and other diseases of undiscovered germs are almost unanimously regarded as infectious on account of general characteristics. The alternate theory that the cancer cell is its own germ, while supported by considerable authority, is, when analyzed, not materially different from the claim that a man can lift himself by his own boot-straps. Whether the malignant diseases are held to be infectious or not there is no general established principle which enables us either to affirm or to deny that malignant involvement of different types of cells is due to the same essential cause and hence constitutes one disease. Conversely, it is equally impossible either to affirm or to deny that there is one essential disease, carcinoma, including epithelioma and cancer of various types of epithelial cells. Thirty years ago much was written regarding the distribution of disease according to embryonic layers. The easy generalizations at first suggested were shown to be inaccurate and the whole subject deserves careful review in the light of modern methods and accumulated knowledge. If cancer, involving epiblast and hypoblast, is essentially one disease, there may also be a unity with sarcoma affecting mesoblast, and, on the other hand, neither

unity nor severalty necessarily depends on this argument. Valuable hints could be obtained even from statistics regarding the joint or sequential occurrence of different types of carcinoma or of carcinoma and sarcoma or of other essentially malignant processes. Reports of such a nature are surprisingly few. The writer has seen pyloric cancer occurring ten years after an extirpated breast cancer and has encountered a very few analogous reports. Just enough cases of this kind are on record to prevent a negative conclusion and not enough to warrant a positive one. However, the extreme rarity of such concurrences or sequences should not influence our general conclusion. Most of the so-called malignant diseases, aside from carcinoma, are extremely rare, even sarcoma being by no means common. The marked and fairly prompt fatality of the malignant diseases in general reduces the possibility of an occurrence of two types in the same individual to an almost infinitesimal proportion. For example, considering the ages at which sarcoma, on the one hand, is common in the sense of an incidence well within 1 per cent. and at which carcinoma is common in the sense of 10 to 20 per cent. of those dying at a given age, the chances of a survivor of the former being attacked by the latter disease is very small, much smaller than might appear from a direct application of the law of chance, for we must consider also the intermediate deaths from intercurrent causes. Even the application of the law of chance to the far commoner types of carcinoma as at present designated in a broad sense is, superficially, only about 5 per cent. of the 10 per cent. that recover at the most, and scarcely 1 to 1000 with due allowance for intercurrent deaths. Supplement this small proportion with the difficulties in the way of obtaining accurate clinical histories and securing their availability in statistical form, and it will readily be seen that the problem is extremely difficult. Yet the actual observation of malignant cases is at times sufficient to warrant the expectation that the problem is soluble, at least in a negative sense. For example, Kolb[1] reports on cancer observed in Bavaria, 1905-07, as follows: Males, 877 malignant tumors, including 288 sarcomas (3.28 per cent.); females, 11,266 malignant tumors, including 300 sarcomas (2.66 per cent.). The care with which the statistics were gathered is indicated by the fact that the location is unspecified in only 196 males and 286 females. He makes no note of carcinoma and sarcoma occurring in the same individual. In passing, it may be remarked that the volume of mesoblastic tissues is enormously greater than that of either hypoblastic or epiblastic or both. This has no special bearing on the question of the identity or non-identity of the two diseases as the resistance of various tissues to well demonstrated infections, such as diphtheria, pneumococcus disease, etc., is equally marked.

[1] Ztschr. f. Krebsforsch., 1910, vol. viii.

THEORY OF RESTS. Inspection of the statistics mentioned shows almost at a glance that the vast majority of cancers occur in organs in which epithelium in the strict sense, hypoblastic or epiblastic, is frankly available. The exceptions are as follows:

	Males.	Females.
Spleen	3	4
Peritoneum	164	531
Pleura	32	33
Kidneys	67	45
Lymph glands	17	7
	283	620

Of course, the occurrence of cancer in an organ containing epithelium does not directly discredit the theory of rests, and it is plausible to believe that they would be more common in tissues of the same kind, yet the theory would receive much stronger support from the frequent occurrence of cancer in organs in which either epiblastic or hypoblastic cells are not normally present. But it is not merely the general rarity of cancer in non-epithelial organs which militates against the theory of rests. The peritoneum, pleura and kidney which account for the large majority of this list of cancers are questionable in a double way. It is not absolutely established whether endothelial cells (a most ignorantly coined word etymologically) and those from the genito-urinary cell mass are mesoblastic or not, and hence, whether the cells can or cannot be properly included as epithelial and their malignant degeneration as cancer. Aside from this point, the great preponderance of peritoneal cancers in women strongly suggests that they were not primary but arose from the genital epithelium well known to account for the general preponderance of cancer in women, while the possibility of error in designating a lymph node as the primary seat of cancer needs only to be mentioned, especially considering the fact that secondary involvement is almost invariable. With these qualifications the numbers presented are too small to support any contention. It must not be forgotten, however, that even it if were shown that all true cancers occurred primarily in organs containing epithelium, as the vast majority certainly do, this would not absolutely disprove the theory of rests.

EPITHELIOMA. Without absolute statements as to identifications, the following cases may be considered as in all probability epithelioma, involving epiblastic cells:

	Males.	Females.
Skin of face	4	5
Other skin	13	24
Head	146	185
Neck	42	29
Trunk	21	34
Extremities	25	29
	251	306

2.95 per cent. males and 2.67 per cent. females of all cancers, excluding sarcoma.

It is scarcely likely that the designation or failure to designate "skin" as a localization has any significance, except in a few cases, aside from the group of cases included under "head" where involvement of muco-cutaneous and mucous membrane and of certain interior structures is probably a considerable factor. The paucity of cases in the groups plainly implying skin involvement in the great majority of instances may perhaps be taken to indicate two important facts, though the probability of greater resistance of dermal epithelium and certain other qualifications must be taken into account. These facts are the relative lack of importance of traumatism in either the chemic, thermic or mechanic sense, in the etiology of cancer and the absence of an infectious agent susceptible of development by direct implantation. While the skin of the body generally may be regarded as protected by clothing from both of these etiological factors, that of the face, hands and neck cannot be. In particular, if traumatism and exposure were appreciable factors, we should expect a notable incidence of cancer of the face in men, from shaving, and a notable excess of cancers of the neck in women from relatively greater exposure. Incidentally, allusion may be made to a statement that I have seen somewhere, to the effect that 1 per cent. of all deaths, not merely from cancer, were due to skin cancer, in spite of the facilities offered for early diagnosis and extirpation. This statement is surprising if true.

Relative Susceptibility of Epithelial Tissues. It would be interesting to know the relative susceptibility of each organ proportionate to its vulnerable tissue. In the absence of anything approaching accurate figures the following approximate estimates may be given. The area of the skin and of the mucous membrane of the alimentary canal is about the same—15,000 sq. cm.—but in males the former has 2.956 per cent. of all cancers, the latter 74.6 per cent. In females the respective ratios are 2.674 per cent. and 50.2 per cent., or, excluding genital and mammary cancers, to make a fairer comparison and revising the percentage basis accordingly, the ratios are 3.7 and 69.4 per cent. In other words the susceptibility of the internal (not entirely hypoblastic) epithelium is twenty to twenty-five times as great as that of the skin. How far the two areas compare in number of cells or mileage of tubules is not known.

For the solid organs a similar but not closely analogous comparison may be made thus:

	Liver.	Pancreas.	Both kidneys.	Thyroid.
Weight, ounces	48 to 58 males 40 to 50 females	3	9	1
Percentage of all cancers, males	6.3	0.6	0.9	0.3
Same, females	7.2	0.5	0.5	0.5
Same, females, adjusted to male figures by excluding genital and mammary cancers	9.9	0.7	0.7	0.5

It appears, at first sight, that there is some approximate relation between the size of the organ and the incidence of cancer, but closer consideration fails to show anything like a close approximation for the smaller glands while the apparent proportionate incidence for the liver is probably due to the well-explained development of cancer subsequent to that of the pylorus or adjoining parts and to the inability to distinguish in statistics between secondary involvement of the liver and true primary growths.

A comparison of the liver and the brain, organs of approximately the same weight and far larger than any other viscera, shows about a tenfold higher incidence in the former, but subject to the same qualification as to the distinction of primary and secondary growths. In the brain about 0.9 per cent. of male cancers and about 0.6 per cent. of female cancers occur. But the physiological conditions are obviously very different, the epithelium of the brain is epiblastic, that of the liver hypoblastic, and the epithelium of the brain highly specialized and not so voluminous in proportion to the total bulk of the organ. Moreover, brain tumors include a disproportionate number of sarcomata and variously classified neoplasms, for which allowance in collated statistics of large series cannot well be made.

The following estimates have been made of the incidence of cancer in various parts of the alimentary canal:

	Area in sq. cm.	Males.	Females.	Females exclusive of genital and mammary cancers, per cent.
Esophagus	50	4.2	1.1	1.5
Stomach	1960	55.2	38.3	52.9
		0.5	0.2	0.3 stomach and esophagus.
		3.3	2.8	3.9 stomach and liver.
		59.0	41.3	57.1 stomach including extensions.
Duodenum	340	5.7	4.9	6.8 intestine except rectum.
Rest of small intestine	8800			
Large intestine to rectum				
Rectum	300	5.7	2.9	4.1

Other approximate estimates have been made that, roughly speaking, gastric cancers outnumber intestinal cancers 10 to 1 and that cancers in or near the rectum outnumber those of the rest of the intestine in about the same ratio. The writer's personal experience scarcely coincides with the above indication of the much greater frequency of esophageal cancers in the male. In approximate correspondence with area of epithelial surface it will be noted that the esophagus is at least as liable to cancer as the stomach even if we ascribe borderline cancers to the latter and consider female statistics, while, if we consider male statistics and give the benefit of the doubt to the esophagus, the proportionate incidence is nearly three times as great for the latter. A similar comparison shows that the rectum may be said to be from a little more susceptible than the

stomach up to twice as susceptible. On the same basis of comparison the stomach, with approximately one-sixth the epithelial area of the intestine, has eight to ten times as many cancers, or, in other words, shows somewhere from fifty to seventy times as much susceptibility. No larger statistical series that the writer has seen distinguish accurately enough between cancers of different parts of the intestine to enable even an approximately accurate arithmetic comparison to be made, but, considering the general acceptance of the rarity of cancers between the duodenum and the rectum, or, at least the lowermost part of the sigmoid, it is not far from the truth to say that the parts of the alimentary canal subject to alkaline digestion show a susceptibility of about one-hundredth that of the parts subject to acid digestion and acid fermentation. But this is not the only factor to be considered. The esophagus, for example, is highly liable to thermic, chemic and mechanic insults, but, on the other hand, is protected by a copious and tenacious mucus, not to mention the differences in cellular histology. With rare exceptions of unusual nature the intestine is entirely free from thermic traumatisms, only rarely subject to mechanic insults or even to chemic irritation beyond those inevitable to its own physiology.

Relation of Sex to Cancer. It has been commonly held that while a somewhat higher incidence of cancer occurred in females, this was mainly on account of the special vulnerability of the sexual organs, including the breasts, and that there was a reduced proportionate incidence of cancer of other organs in the female, perhaps not quite balancing the strictly sexual cancers, but nearly so. It is possible to juggle statistics in various ways, and, even without intentional bias, to arrive at somewhat different interpretations, according as we do or do not take account of the slightly different proportionate numbers of males and females in a given population, according as we estimate death-rates according to general population or that of age groups or compare deaths from a given cause, for example, cancer, with all deaths in the same age group or other unit. Again, as pointed out especially in an article in the *Med. Record*, April 18, 1914, males and females die at different rates in different age groups, there being for most areas an initial higher birth of males and a correspondingly higher number of male deaths until sexual differences, primary and due to habits of life, afford strictly sexual reasons for death. In this country especially, and perhaps almost exclusively, on account of immigration, males predominate in the population, though an exception exists in the case of several Eastern States from which males have migrated in considerable numbers to the West, so that there is a preponderance of male deaths until the age group seventy-five to seventy-nine. Thereafter there being an excess of old women over old men and the duration of life being obviously short, deaths of females are in excess.

Again, for a considerable period of middle and rather advanced life, the mortality rates for men in any given age group compare more closely with the next or the second junior age group for women, while, at extreme ages, there is a tendency toward equalization. Thus, for anyone who really tries to make a fair comparison, the problem is quite complicated. But however one attacks the problem, it appears that the commonly accepted idea of the influence of cancer of the sexual organs on the total cancer incidence of the sex is erroneous. For example, if we subtract the sex organ (including mammary) cancers from the total cancers of women, as indicated by the actual number of deaths, we find fewer female than male cancers, for any recent census year in the United States. But the difference is almost exactly the same as that between male and female deaths in general and is nearly proportionate to the excess of males in the population, which, in turn, is due mainly to the excess of immigration of males. In other words, if we eliminate for the moment all consideration of cancer of the female sexual organs (including the breasts) the cancer deaths and undoubtedly the incidence is almost exactly the same, proportionately for the two sexes. The proportionate occurrence of cancer in various organs aside from the sexual is not quite the same for the two sexes, but, in general, there is not a great difference, and especially not for the organs of maximum incidence, although there are some details more or less explainable, as the notably smaller incidence of buccal cancer in females (better care of mouth and teeth, less irritation from smoking). Cancer of the sexual organs of the female may therefore be regarded as an element added to an approximately equal incidence for other organs.

Locus Minoris Resistentiæ. If we regard this principle as meaning that an individual is, for various reasons, to be infected or affected with a given disease somewhere and that the localization alone is to be determined by local conditions, permanent or temporary, the above fact may be interpreted as an argument against the conception that cancer is a general disease. That is to say, if merely the location of a cancer depended on local conditions the excessive liability to cancer of the sexual organs in females would, as is generally believed, lessen its incidence in other organs, which is in general not true. It is scarcely necessary to state, however, that this conception of *locus minoris resistentiæ* does not apply to any disease. Thus there is sound reason for regarding cancer not as a condition to which an individual is doomed by law of chance or by extrinsic causes and that the cancer, being obliged to locate somewhere is, so to speak, attracted to one or another organ but as a disease, whether infectious or not, whose development depends upon susceptibility of the part in which it actually does develop. In this sense it must be granted that cancer is at the beginning a local process. But like various other diseases necessarily having a

lesional location, it is also general. One need not repeat the argument as to the general nature of diphtheria, pneumonia, etc. The conception of cancer as a local process must also be qualified in a narrow but very practical sense. Even dermal lesions which offer the best opportunities for early diagnosis and relatively accessible but more or less concealed cancers cannot, under present conditions, be successfully eradicated in more than a quarter of cases even when their destruction is resorted to promptly.

CAUSE. As stated there is at present no direct evidence of a germ and no indirect evidence, geographic, racial, dietetic, etc., pointing to any definite extrinsic cause of cancer. Except by analogy from neoplasms of the lower animals which are not necessarily identical with human cancer, even though histologically similar, there is no valid evidence of a specific infectious element, such as exists without reasonable doubt for various diseases, including several exanthemata of undiscovered germ. The word germ, by the way, is used without apology, to indicate the broad nature of the etiological problem in this regard. The development of cancer seems to depend upon the susceptibility of a special part of the body but no plausible predisposing cause, as age, *per se*, or as indicative of metabolic changes, traumatisms, gross or mild and repeated, preëxisting non-cancerous lesions, general state of depression or bad hygiene has, so far, been satisfactorily reduced to the "with or without" test. That is to say, no plausible cause assigned as favoring the development of cancer in a given case, necessarily has the same result in all or even the majority of cases while, on the other hand, cancer of any part may develop without any of the plausible causes used to explain other cases. In plain words, we cannot prophesy with more than a small chance of fulfilment that any exposure or lack of caution, or antecedent disease, will result in cancer. The proportion of fulfilments is indeed so small that we can scarcely regard it as more than a coincidence. About the only advice we can give to prevent the development of cancer, and even then without absolute assurance, is not to subject any part to a repeated irritation of any kind, not to bear children, and to die before the age of forty.

IMMUNITY AND SUSCEPTIBILITY. It has been well established that heredity plays no notable part in cancer. Given a large family in near generations, or, what really amounts to the same thing, a familiarity with family history, almost any cancer case will afford a history of cancer in the family. Otherwise, instances of apparent family tendencies are shown to be pure coincidences by the sporadic occurrence of other cases without similar family history. There is no evidence that anything approaching specific immunity explains the incidence or non-incidence of cancer. So far as can be judged, its occurrence is either according to the law of chance or due to local susceptibility. As previously implied, if it could be shown

that a cured case was immune, very definite conclusions could be drawn. But, on the one hand, the chance of a subsequent independent involvement with cancer of a case from which cancer has been removed and which has survived for a sufficient length of time to warrant a belief in cure, is very slight, so that the infrequency of such cases is no argument for the acquirement of a true immunity; on the other hand, that such cases occasionally occur shows that such an immunity is not absolute.

HEART MUSCLE EQUATIONS.

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To the average general practitioner—in fact, to many of us who considered ourselves internists—the recognition of myocardial disease depends almost entirely upon evidence either of marked arteriosclerosis or upon the presence of irregularities in the heart-beat. The teaching in the schools does not go beyond this point. That a man might be free from symptoms, have sufficiently good cardiac compensation for the needs of his daily life, might have a normal blood-pressure, no signs of an arteriosclerosis and no irregularity of the pulse, and yet might have a serious defect of his myocardium, is generally not recognized. The mass of data accumulated during the war has given a new insight into this question. Dealing, as we did at Camp Greenleaf with men who were in general above draft age, a great opportunity was presented for the study of lesions of the myocardium.

While the methods of examination are those in use in a cantonment, as applied to men under military control, slight modifications in the type of exercise prescribed between examinations of the patient and the use of tact in employing the functional tests should make the methods of equal value in civil practice.

In order to have a clear idea of the factors concerned in determining the "work value" of the heart, mention of some of the well-known points in cardiac pathology and physiology may be worth while. Any infectious process, whether it be tonsillitis, pneumonia or "grippe"—which is usually a streptococcus process—scarlet fever, typhoid fever, diphtheria, as well as the better recognized etiological factors—rheumatic fever or syphilis—can and usually does cause some damage to the heart in greater or lesser degree. These infectious processes, of whatever sort, leave behind, as a rule, a point of least resistance in the heart; hence, not only is the chance of further

damage to the heart greater with each succeeding infection, but since the action of the disease is, to a certain extent, selective in its attack upon the cardiac tissues, a recurrent infection of a particular variety is more to be feared than is infection with a variety of different diseases. For instance, repeated attacks of rheumatic fever will generally show a greater effect upon the heart than would have been the case had the individual had but one attack of rheumatic fever, and, at other times, pneumonia and scarlet fever. Of particular importance from the point of view of eligibility for army service is the fact that some of the chronic disease processes in the heart tissue are, regardless of further infection, cumulative in their action; in other words, the end-result of a series of bacterial invasions of the heart progresses of itself in severity with the passage of time, from a process which at first was of little importance to a disabling condition. Finally, and by far the most important fact of all in the practical application of cardiac pathology, a fact frequently ignored on the part of physicians, there is, usually, an involvement of the heart muscle in most infections of the organ. We have been accustomed to consider the damage that these diseases do to the heart merely in terms of the endocardium—in particular to the valve segments—when, as a matter of fact, the valve defects produced were in many cases of less far-reaching consequence than the damage to the myocardium that went hand in hand with the endocarditis. Above all else in the estimation of the capacity of the heart muscle to do work, this fact—namely, that infectious diseases do, as a rule, produce damage to heart muscle and that this resulting damage to the myocardium is, as a rule, not discovered until much later than the accompanying valve defect must be borne in mind, for it is absolutely fundamental to the conception of the problem.

We know that if the heart muscle be fully competent its reserve power is so great that even a very serious valve defect, such as a mitral or an aortic regurgitation of marked grade, can be overcome by the intact muscle without any backing up in the lesser or in the greater circulations respectively. In the same way a normal heart muscle will compensate by hypertrophy for the work necessary to overcome the resistance of a narrowed valve opening. Up to an indeterminate point the heart valves may be very seriously damaged without any break in compensation if the power of the pump is undiminished. Hence, for the quantitative and qualitative estimation of the power of a particular heart we must consider as factors in the reverse order of their importance (1) the valvular defect if any; (2) the maximum work required of the heart, and (3) the competency of the heart muscle.

Taking the criteria as to the condition of the myocardium in the order in which we reach them during the routine examination, we may lay stress, to a greater or less degree, upon the following: (1) Blood-pressure determinations; (2) the quality, rate and volume

of the radial pulse; (3) the force of the apex impulse; (4) the length, loudness and quality of the first sound at the apex; (5) the presence and character of the second sound at the apex; (6) the character of the sounds over the lower part of the right ventricle and the comparison of the sounds at this point with the sounds at the apex; (7) the effect of exercise upon the quality of the first and second sounds at the apex and over the right ventricle, with a comparison of the sounds at these two points; (8) the "effort test," as such, with relation to pulse-rate, dyspnea, cyanosis, cough and distress; (9) the presence and quality of the sounds at the base; (10) the presence or absence of relative signs of cardiac decompensation, such as edema at the bases of the lungs, edema of the extremities and the causation, as a result, of exercise of a systolic murmur at the apex, not to be heard before exercise; (11) the presence or the increase as a result of exercise of irregularities in the heart-beat; (12) various formulæ for the determination of cardiac power by means of exercise, blood-pressure readings, pulse-rates or by combinations of these factors.

While in some instances a more thorough conception as to the condition of the heart muscle might be obtained through the use of the electrocardiograph or the polygraph, these instruments are often not available, and they are by no means indispensable to a very accurate determination of the function of the heart of a given person.

Two simple facts upon which I wish to lay particular stress are these: (1) our problem deals with a complex human mechanism and not with a machine; hence, it can never be reduced to the terms of machinery, and errors are bound to occur at times; (2) if sufficient time is taken and a sufficient number of observations are made in cases of doubt, very few errors will be made. In a large percentage of cases thoroughly accurate and satisfactory work cannot be completed under a week or ten days.

The routine, when the necessity for speed in the completion of the physical examination has not shortened the examination to a period insufficient for the best work, is as follows: The systolic and diastolic blood-pressures are taken with a mercury instrument, the subject being in a sitting position. The pulse-rate is then counted with the man standing, the quality of the pulse wave and the condition of the radial artery determined, and if there is present any tachycardia, or in cases in which it is desired to make the standard "effort test" of the Army, as prescribed for draft boards, the pulse-rate is again taken with the subject recumbent. The location of the apex-beat, percussion of the borders of cardiac dulness and auscultation over the apex, over the tip of the right ventricle, along the line from the apex to the aortic area and over the pulmonic area, is made in the usual way. Suspicious sounds are listened to with the subject recumbent, and he is then tested as to the work coefficient of his heart muscle in either one of two ways. The "effort

test," as laid down for the draft examinations, requires that a man shall hop 100 times in succession upon one foot. This test is thoroughly effective, and although the work done by one subject will differ from that done by another to a degree greater than is the case when using the "staircase test," because one man will hop higher or will bend his knees more than another, yet this disadvantage is outweighed by the economy of room, of time and of apparatus. When used to determine the presence or absence of the "effort syndrome" the pulse-rate is taken in the recumbent position, and the subject then takes the 100 hops, the pulse-rate recumbent being taken again immediately. Normally, after 100 hops the pulse recumbent should return inside of two minutes to within five beats per minute of the preëxercise rate. If the pulse returns within these limits of time and rate the effort test is said to be normal for that individual and the so-called "effort syndrome" is thereby excluded. In dealing with older men, with men who are, as a rule, flabby of muscle and who are being examined more with regard to the competency of the myocardium than for the presence of an "effort syndrome," a somewhat different procedure is followed. While perhaps in many cases the completion of the standard test might give us some information, yet, in so far as the heart muscle is concerned, there is much less to be learned from the heart-rate, particularly in dealing with nervous individuals of middle age, than from other phenomena; and since few men of middle age, physically untrained, are able to complete the 100 hops without exhaustion and the risk of actual damage to the heart, these same men will show up any deficiency in the power of their heart muscle with a much smaller amount of exercise *in most cases*. Usually, I request the candidate to hop upon either foot until I ask him to stop; and he is made to hop 20 to 40 times, depending on his age and weight or until he seems to be tiring. When the man completes his full 100 hops he has done an amount of work that is almost certain to bring to light any defect in his heart, whereas, in a few cases, the compensation in a particular individual may lie, let us say, in the neighborhood of 60 hops; if he be made to hop 80 times he is certain to exhibit proof of decompensation, which will be overlooked at the end of only 40 hops, because for this individual 40 hops are below the limit of the reserve power of his myocardium. Hence, this is a source of possible error. Another possibility with the effort test as concerns the chance of error, lies (1) in the fact that graduated exercise may increase compensation to a point above the ordinary demands upon the cardiac reserve—in which case we may consider such a heart to have reëstablished its title to our full confidence; and (2) in the fact that rest may build up the reserve of a seriously weakened myocardium to a point where it is able to stand a limited amount of work, and apparently to prove itself above suspicion through an apparently good effort test, although the seeming change

in the muscle is in reality of only brief duration. This last type of error can be almost automatically avoided by a sufficient period of probation and by making the function test—the ability to withstand the strain of repeated graduated exercises—of a less severe type than the hopping test.

To return to the routine examination: One has the candidate exercise by hopping and then one listens to the sounds at the apex, over the right ventricle and at the base, as before, comparing the first and second sounds with each other at each point; also comparing the quality of either sound at one point with its quality at another point. One considers not only the quality of the sound but also whether any murmurs, inaudible before exercise, are now to be heard. Sometimes the patient is then reauscultated recumbent. Under these procedures cases fall into one of three classes: Those coming within normal limits; those who will not be injured by a moderate amount of graduated routine exercise, such as setting-up exercises and company drills; and those definitely unfit for active exercise at the moment. In the determination of these categories the age, the weight, the habits as to exercise and the possibility of a recent attack of an infectious disease must be taken into consideration. Those cases fit for drill and not in the "normal" class are allowed to do all of their company duties short of violent exertion for a week, returning at the end of that time for a reëxamination exactly like the first; and if the disposition of the case cannot then be determined, they return again two days later. Those cases not fit for drill are reëxamined at two-day intervals until the condition present is self-evident. In all abnormal cases it has seemed to me that at least one reëxamination was essential, as any heart case, whether the defect be of the myocardium or of the valves, will change in physical signs from day to day; and since most of our candidates were nervous regarding the examination, had just completed a long journey and were usually suffering from constipation as the result of the change in living conditions, a much fairer picture as to the true condition existing in the heart could usually be obtained on the second examination.

Taking up the points of greater or lesser value in the estimation of heart power, let us start with the determination of systolic and diastolic blood-pressure. Later on I shall discuss some of the various formulæ used with the blood-pressure readings as factors; but to begin with, I shall take the single determination, in the sitting position before exercise, of the systolic and diastolic readings. Incidentally, after personal use of the spring instrument for many years, I have had an opportunity to rediscover the mercurial manometer, with a great deal of satisfaction. As I pointed out in a previous paper on the physical examination of recruits[1] with men of the educated classes, and especially with those who are at all nervous, the systolic blood-pressure is usually elevated. How much of this

is due to a recent long journey, to the change in environment, to the habitual constipation from which, in my opinion, practically all physicians and others of sedentary habit suffer, or to pure nervousness, I do not know. Since there is a limit to the amount of very strong thein or caffein and tannin decoction which a man can imbibe, and since the drinking of water falls off very greatly in cold weather, since also the urines in these examinations showed an almost invariable increase in specific gravity—averaging 1.026 to 1.040—to such an extent that my impression of the average specific gravity found at Camp Greenleaf, was that it lay in the vicinity of 1.030—I feel that constipation, habitual or recent, plus a decreased fluid intake, is responsible for the elevated systolic pressures, at least in many cases. What we must, I think, admit is that we actually know very little as to the significance for good or ill of either the systolic or the diastolic pressure. While I believe that a systolic pressure of over 150 or under 115 indicates some condition—probably either a toxemia or a change in internal secretion—unfavorably affecting vasomotor control, and that the redetermination of the pressure and a search for the cause thereof should be made, I do not feel that there is any definite proof as to the power of the heart muscle contained in the single determination of systolic and diastolic pressures. Many observers hold that a diastolic pressure of over 100 indicates a myocardial defect. I cannot see the facts in that light. Who has any proof as to this or any other theory regarding blood-pressure? My contention is, if we admit, as many observers do, that a systolic pressure of 160 may be perfectly normal for a man, aged fifty years, and that the diastolic pressure should maintain its relationship with the systolic, approximately in the ratio as two is to three, then with a systolic pressure of 160 we ought to expect a diastolic pressure of 105 to 110 as a normal counterpart to the systolic pressure.

In a particular individual the apparent size of the radial artery, the volume of the pulse wave and the tension of the pulse depend to a very great extent upon the conformation of the arm and the degree of adiposity of the individual. Hence, while the force of the pulse is a good indication as regards a recent infection, and may help us in the diagnosis of an acute myocarditis, it is of much less value than is the blood-pressure reading as regards the heart power. The volume of the pulse, other than in so far as it shows individual variation, is of help only in the diagnosis of a valve lesion, or in estimating the change in conditions in one subject from day to day. The pulse-rate may be either a help or a hindrance in visualizing heart force. A rapid pulse-rate may indicate nervousness, irritable heart action, an active absorption of toxins from a lung focus—either tuberculous or otherwise—from the tooth sockets, nasal sinuses or the intestine, or perhaps a thyroid hypersecretion; or, on the other hand, it may be the only sign left of a pancarditis,

originally involving the heart valves as well as the myocardium. Cases have been frequent here, where there was a persistent tachycardia, associated with a very slight involvement of the mitral valve, either with signs of a very slight stenosis or regurgitation, with a good response of the heart to work tests, and no other indication of fundamentally serious damage to the heart except the frequency of the pulse. Judging from my observation of children who at one time had definite disease of the mitral valve, and who some years later showed no signs whatsoever of the valvular condition, but who did have this same tachycardia, I am inclined to believe that, as the only sign of a damage to the myocardium of slight extent, a rapid pulse-rate is much more common than it is supposed to be. The use of the pulse-rate in the estimation of the work efficiency of the heart I have already discussed.

The force of the apex-beat is no safe guide as to the capacity of the heart for work. A thick chest wall will often cushion the apex push of a competent heart; a dynamic heart action or an hypertrophied although seriously damaged myocardium will give us, on the other hand, a very forcible impulse. Here, the existence of emphysema of the lungs may play a part in the result.

The length, the loudness and the quality of tone of the first sound at the apex is of great importance. In the case of a normal heart muscle the first heart sound at the apex has a forceful, muscular tone, and is of a good length. If the first sound at the apex becomes "booming" in character it usually indicates increase in the work demanded of the heart, and one usually finds present either an hypertrophy of the heart, an increased blood-pressure or an increased aortic second sound. It is my profound conviction that all of the signs just mentioned—hypertrophy, hypertension and increased aortic second sound—combined with a moderate cyanosis, can be produced, and are very often so produced, as the result of a chronic intestinal stasis, even when the individual is having a daily bowel movement. They, of course, occur frequently in thyrotoxicosis. As was mentioned in the case of the apex-beat there are several conditions other than weakness of the sound, which may make the first sound at the apex seem weak. This may be due to the mere physical distance of the apex from the stethoscope, either from the thickness of the chest wall or the presence between the heart and the ear of emphysematous lung. Sometimes it may happen that the heart merely swings away from contact with the chest wall, in which case, by getting the subject to bend forward so as to place the heart in the closest possible contact with the chest, one will at least have the best possible conditions for auscultation. Quite often the heart sounds are almost inaudible except at the base of the heart. As a rule, this is the case only in large elderly men with a slow pulse, or at least a pulse that is not rapid. When the heart sounds are so very distant our examination is almost com-

pletely limited to the effect of exercise on the pulse-rate and upon the heart sounds. If the response to exercise in these two respects conforms to the criteria which will be described later, then we may safely assume, according to my experience, that the individual has the necessary heart power even if the heart sounds when he is at rest seem disconcertingly vague and distant.

In my opinion neither a mere "roughening" of the first sound, ending with the end of the first sound, nor a reduplication of the first sound, which is to be differentiated from a presystolic murmur by the absence of the crescendo pitch and the abrupt ending of the latter, detracts from the muscle quality of the sound, and they are to be noted merely to differentiate them from murmurs.

Do most of us give much thought to the second heart sound heard at the apex except in so far as it may be double or may be accentuated, both of which conditions merely suggest a possible mitral stenosis? It was not until I had been experimenting on the work value of the heart for some months that I became interested in the weakness or absence of the second sound at the apex of the heart. What is the cause of the presence or the absence of this sound, which, of course, is propagated to the apex from the base of the heart? Opinions seem to differ on this point, some observers believing that the position of the heart and the conditions of the lungs as regards emphysema are responsible for the absence of this sound at the apex. My own view is that, barring marked emphysema, the second sound can usually be heard at the apex if the subject be made to bend forward, and that a failure to hear this sound indicates a defect in transmission from the point of origin, presumably with an accompanying muscle defect. Whether the second sound heard at the apex is the aortic or the pulmonic sound, or both, or whether it may vary in different individuals or in the same individual at different times, depending upon the preponderance of the aortic or of the pulmonic second sound, I have not determined to my satisfaction. Of only one thing in this connection do I feel certain: If the first sound at the apex, and with the subject leaning forward, has not become appreciably more distant as the result of exercise, as sometimes happens in marked emphysema, then the second sound at the apex should be audible after exercise. Failure in the quality of the second sound after exercise, even with the subject bent forward, indicates to me a defect in the myocardium.

Another valuable standard as to the interpretation of the sounds at the apex, and one which is peculiarly adaptable for reference in each particular case, since each man carries his own standard with him, lies in the comparison of the sounds over the tip of the right ventricle with those heard over the apex. This observation was first pointed out to me by Le Roy B. Crummer, of Omaha. The best point at which to listen is usually about an inch and a half to the right of the apex, roughly, in the fifth space at the left sternal

margin. Normally, the sounds over the right ventricle at this point are much less loud and are more distant than those at the apex, but normally the first and second sounds are heard well at this point. While as the result of disease the sounds here may share equally with those at the apex in the loss of muscular quality of the first sound and the clearness of the second sound, yet the damage to the left ventricle may be much greater than to the right or the change in the sounds may be due to emphysema. In any case, without marked emphysema, if the sounds over the right ventricle, and in particular if the first sound at this point is louder than the first sound at the apex, it indicates, I believe, a loss in the muscle tone of the left ventricle.

Stress has been laid on the importance of the quality of the first heart sound at the apex with the subject at rest. Much more important information is to be obtained from a study of the first sound after the subject's heart muscle has been put through its paces by means of the effort test. *Exercise should increase the clearness with which the heart sounds are to be heard,* except in the presence of a marked large-lunged emphysema. The first sound at the apex should improve in loudness, in length and in sharpness as the result of work. The second sound at the apex, if audible at this point before the effort test, should be increased by this procedure, in my opinion, if the muscle be of good capacity and there be no marked emphysema. If, as a result of exercise, either the first or the second sounds at the apex lose in quality, in loudness, in distinctness, I believe that, in the absence of an emphysema, we have proof of a defect in heart-muscle function. Whether the enfeeblement of the second sound at the apex after exercise be due to a change in the relative accentuation of one or the other second sounds at the base, to a change in the force of closure of both pulmonic and aortic valves, or to a change in the conductivity of sound on the part of the heart muscle, does not, to my mind, alter the significance of a weakened second sound. Also of very great value, I believe, is the comparison of the relative strength, or loudness, of the sounds at the apex and the sounds over the right ventricle as affected by exertion. As stated above, the sounds, both first and second, are normally louder over the apex than over the right ventricle when the man is at rest. This relationship, to my mind, should also hold good after the work of the heart muscle has been increased. If the sounds over the right ventricle, as the result of the effort test, become more accentuated than those at the apex I feel that this would indicate either an enfeebled power of the left heart or a backing up in the lesser circulation increasing the work of the right heart, whichever way one wishes to state the case. While it is, of course, conceivable that a marked emphysema should make the heart sounds more distant after exercise, yet with a condition marked enough to do this the interposition of emphysematous lung between the heart and the

chest wall should work equally over the apex and the right ventricle; hence, I do not consider that emphysema should cause an increase in the sounds over the right heart at the expense of the sounds at the apex. Here, again, in comparing the sounds at these two points, one should remove all possible source of error by having the subject bend forward.

Perhaps the most important evidence of all in estimating the cardiac function is provided by the production of symptoms as the result of the effort test: (1) Dyspnea is to be considered. Here a certain amount of caution is to be observed. Increase in heart work, with its increase in pulse-rate, will, of course, produce a certain degree of increase in the rate of respiration; if this stops short of markedly rapid breathing we cannot speak of dyspnea. With real dyspnea there should be more or less actual air hunger, as evidenced by a deeper breathing, use of the accessory muscles of respiration or movement of the alæ nasi. In other words if the circulation is really embarrassed we should have some signs of distress. There may be present a flushing of the face, and some increase in cyanosis may occur as further evidence. Provided that there is not some self-evident process present in the lungs, the causation by exertion of an irritative cough is also presumptive proof of lack of power on the part of the left heart. One symptom, not ordinarily thought of and not referred to in the literature as a sign of fibrous change in the myocardium, is the production, with or without other signs of decompensation, of a high degree of exhaustion, with an accompanying lassitude of surprising severity, out of all proportion to the amount of exertion needed to produce this symptom. While in the military service such statements must be taken with reserve, in private practice I feel that the complaint of undue exhaustion from such every-day occupations, as carrying moderately heavy weights, running for a street car or putting a tire on a car, should be viewed as of considerable importance, both in the diagnosis and in the treatment of a weakened heart muscle. While, as stated before, the full "effort test" is not, as a rule, gone through with, one can judge accurately enough in most cases as to the effect of work upon the heart rate by observing the degree of acceleration of the pulse after 20 to 40 hops and the promptness with which the heart action again becomes quiet. One caution with regard to the estimation of the degree of dyspnea is necessary. Psychic causes, such as excitement, a belief that there is something serious the matter with the heart, a neurotic temperament or a desire to avoid military duty, may all cause a veritable moving picture of dyspnea, with gasping respiration, marked distress and every appearance of utter fatigue, regardless of the severity of the exertion. I suppose that the most stupid of individuals is able to double the rate of his breathing, and often the less real the condition and the more self-pity the individual possesses the more realistic picture of abject exhaustion is he able to present.

With regard to the second sounds at the base not very much information of value regarding the heart muscle is obtainable. While an increase in one or the other of the second sounds at the base is of very great value in suggesting further study of the vessels, of the kidneys or of the lungs, except in so far as an increase of marked degree in the sharpness of the pulmonic second sound at the base suggests a deficient emptying of the left ventricle, no definite weight regarding the myocardium can be placed upon increase in the second sounds at this point. A decrease or an absence of second sound over the aortic or the pulmonic area suggests more a possible defect or anomaly of the valve in question than any change in the muscle function.

It would seem to be self-evident that in the absence of a valvular lesion any evidence of cardiac decompensation is necessarily proof of a defect of the cardiac muscle. Probably no one will disagree with the opinion that the presence of edema at the bases of the lungs or of edema of the ankles is proof of such decompensation. Even here a certain amount of caution is to be observed, as in a given case such decompensation may be purely related to flabbiness and fatty deposit in the heart or to a lack of the habit of strenuous exertion; and these signs may soon disappear after the man has become accustomed to the amount of work which he is required to do. So far as I can see, such must be the case with all heart muscle when taking on greater loads of work than that to which it is accustomed, and it is the purpose of all athletic training to increase the work power of the heart in just this way. Hence, again, a reason why it seems to me impossible to render a just and accurate decision as to the power of a given heart in one examination. Another source of error in respect to swelling of the ankles lies in the fact that the present uniform lends itself to undue confinement of the legs, and that many men, either from ignorance or from vanity, lace their breeches or strap their leggings to a degree interfering with the circulation in the lower leg. This I believe to be the case to a greater degree when a man first enters the service than later on in his military career. The most important sign, in my belief, of a decompensation of the heart lies in the production, as the result of exercise, of a systolic murmur at the apex, there being no murmur audible previous to the effort test. About the significance of this fact there seems to be some difference of opinion; in other words, there is a difference of opinion as to the physiological means of production of this murmur. In practice I think that any murmur which is of cardiorespiratory nature, and which disappears when the subject stops breathing, should be excluded from the type of sound that I am discussing. Personally, I am convinced that where there is no murmur heard at the apex of the heart when the subject is at rest the appearance of a constant murmur, systolic in time, usually short, and following the first sound without pause, the murmur persisting

for a longer or shorter interval as the heart quiets down, is to be accepted as evidence of an acute dilatation of the heart, and that the resulting murmur is due to a relative mitral regurgitation produced by the stretching of the mitral valve ring. Whenever this "breaking" of the first sound into a murmur as the result of the effort test occurs I feel that a diagnosis of a myocardial insufficiency can be made without question. Whether this myocardial weakness is to be taken as evidence of an actual myocardial disease or not depends again upon the previous habits of the individual as to exercise; and naturally enough, more exercise will be required to produce this sign in one defective heart than in another.

Furthermore, the man, although having a relative mitral insufficiency, may have enough muscle compensation to take care of the extra heart work required by this regurgitant stream of blood and may show no sign whatsoever of distress; in exactly the same way that a heart with an actual rather than a relative regurgitation might readily be able to carry the extra load without symptoms, yet in neither the case of the relative nor the actual regurgitation do I feel that we can accept the absence of symptoms as a proof of the freedom of the heart from defect. To my mind the presence of a relative mitral regurgitation without valve lesion, as evidenced by the appearance of a systolic murmur after exercise, is proof of a very definite lesion of the heart muscle.

Irregularities in the heart-beat may or may not be of significance as to muscle function. Ordinarily the occurrence of infrequent extrasystoles, which is the commonest form of irregularity, is of no importance; and, as a rule, under the influence of exercise, the irregularity disappears. When the extrasystoles become more frequent after exertion, or, what is more common, when the irregularity becomes more frequent a few minutes after the effort test than was the case before added work was put upon the heart, this would seem to indicate a considerable degree of change in the heart parenchyma. The presence, whether at rest or after work, of a gallop rhythm, persisting during several examinations, is believed to indicate a grave injury to the myocardium. Among men, especially in those who have been accepted for military service, auricular fibrillation is an extremely rare condition. In the examination in the military service of more than 30,000 hearts, for which I have been responsible, I have seen only two cases of this condition, one of them without concomitant valve lesion; the other of the paroxysmal type, disappearing entirely while under observation. Of course, when present, this condition is of serious import as regards the soundness of the heart muscle. The other irregularities of the heart need not be mentioned in detail, as they are either self-evidently of evil omen, are rarely found, or carry with them other conditions in themselves also serious. One exception that I may make to this last statement relates to simple pauses in the heart-

beat, that is, apparently dropped beats, both at the wrist and over the precordium, in which the polygraph tracing showed a complete pause both in the auricle and in the ventricle. In this condition, of which several very marked cases have been observed in soldiers, there was apparently present a simple sinus arrhythmia of no prognostic or diagnostic importance. While it is not in the ordinary sense an arrhythmia, an alternating pulse, one strong and one weak beat alternating, properly should be spoken of here. It is believed to indicate damage to the myocardium.

In the discussion of the various formulæ for the determination of cardiac function the following are worthy of consideration.

The Staircase Test of Selig. The pulse is counted and the systolic blood-pressure taken. The candidate then ascends twenty steps rapidly, the pulse-rate and systolic pressure being taken again at once. Normally the pulse-rate rises twenty beats; the systolic pressure rises 8 to 10 mm. Selig considered that the time of the return of the blood-pressure to normal was an index of the degree of myocardial defect. This test, or modifications thereof, is much used, but the standard set as to blood-pressure by itself is not of definite value.[2]

Graupner's Blood-pressure Curve. After taking the systolic pressure and the pulse-rate the subject is given a definite amount of exercise, and when the pulse-rate has returned to the preëxercise rate the systolic pressure is again taken. If the systolic pressure after exercise remains constant, Graupner considered the myocardium to be normal. If the blood-pressure falls as the result of exercise the muscle is insufficient; if the blood-pressure rises and then returns to normal there is present compensation of the heart; while if the pressure rises, then rapidly falls and does not rise again the heart muscle is in a state of fatigue.[3] Cabot and Bruce, experimenting with this test, believe that it gives valuable information.[4] Personally, I believe that, while a persistent fall of blood-pressure following exertion indicates in general a possible myocardial insufficiency, there are so many factors outside of the heart muscle entering into the problem that the test is not wholly dependable.

The Cardiac Efficiency Factor of Tiegerstedt. This employs the equation:

$$\frac{\text{Pulse-pressure} \times \text{pulse-rate}}{\text{Systolic pressure} \times \text{pulse-rate}} = \frac{\text{velocity}}{\text{work}} = \text{coefficient of the pumping power of the heart.}$$

The pulse-rate may be omitted from the above equation, leaving merely the relation between pulse-pressure and systolic pressure, normally a ratio of 1 to 3. Tiegerstedt holds that any increase in this ratio whereby the pulse-pressure approaches the systolic pressure represents heart weakness.

The Cardiac Overload Factor. This is practically the inversion of the above. Normally, pulse-pressure is to diastolic pressure

as one is to two. Stone holds the view that the approach of the pulse-pressure nearer to the diastolic pressure represents overload on the heart.[5]

Whether one makes one's equation using the pulse-pressure with the diastolic or with the systolic pressure as the second factor, respectively, does not actually make much difference, since the equations are very likely to be reciprocal, and in many cases no value can be placed on either the Tiegerstedt or the Stone formula. As stated before it would seem that the diastolic pressure should follow the systolic pressure upward, in the normal ratio, except in cases in which aortic insufficiency, hyperthyroidism or "effort syndrome" is present, and that a disturbance of this ratio indicates an abnormal condition, though not necessarily of the heart muscle.

Goodman and Howell's Four Phases of Blood-pressure. The estimation of the length of the four phases of the blood- pressure as determined with a stethoscope over the cubital space, seems to me to be too empiric and too difficult of accurate determination to be a practicable means of judging heart power.[6]

Equations having as factors the pulse-rate and the systolic and pulse-pressures, standing and recumbent, with or without the effect of exercise upon these factors, have in my experience no advantage over the simpler tests and formulæ. After all, all of these formulæ are merely attempts, very praiseworthy and very desirable as such, to solve a problem that does not seem possible of solution by any mathematical equation. If we knew what we were dealing with in studying the question of blood-pressure, if we really knew what any of the factors of which we speak so glibly really meant, if we really knew what caused the changes in any of these factors, then we might be able to make a chart that would show what was to be deduced from a given combination of factors. For example, we do not know what the systolic pressure represents except perhaps the peripheral resistance as maintained by vasomotor control. We say readily that diastolic pressure is the mean pressure, that it is determined by the end of the third phase through the stethoscope, that it represents the power of the heart muscle, but we do not know any of these things as facts.

Conclusions. I. No single procedure or formula gives universally applicable information regarding the integrity of the heart muscle in a given case.

II. In the order of their value as indications of a damaged myocardium, I would place the following criteria:

1. The general appearance of the subject, with special reference to his color, to the occurrence of actual dyspnea, or distress, or cough or exhaustion resulting from exercise.

2. The presence of a true gallop rhythm at rest or following exercise.

3. The production, as the result of exercise, of a relative mitral insufficiency, as evidenced by a murmur.

4. The presence, in the absence of valvular disease, of signs of decompensation, as edema of the lungs or of the extremities, whether at rest or after exercise.

5. Weakening of the first sound at the apex, resulting from the effort test.

6. Increased strength of the first sound over the right ventricle as compared with the first sound at the apex, occurring after exertion.

7. Weakened first sound at the apex, at rest, in the absence of emphysema.

8. The production, following the effort test, of irregular heart action or the increase in irregularity, already present, brought on by exertion.

9. Loss or weakening of the second sound at the apex, due to exercise.

III. Variations in the systolic, in the diastolic or in the pulse-pressures are believed to give relatively little information regarding the cardiac function.

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ADVANCEMENT IN THE TREATMENT OF WOUNDS AND INFECTIONS RESULTING FROM THE WAR.

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What effect will the experiences of surgeons during the war have on the civil practice of surgery? Has the treatment of wounds been revolutionized? Has any new antiseptic been discovered since the beginning of the war which will prevent or arrest infection? Will experience in the treatment of war wounds change our treatment of wounds in civil practice? What have the men who have been working in military hospitals really learned?

These are the questions which one has constantly put to him by members of the profession and by intelligent and inquiring laymen, and, although the answers cannot always be categorical or perhaps satisfying, yet it has seemed worth while, now that the war has terminated, to take stock of our experiences and to try to estimate of what real value they have been. In doing this I shall endeavor to bear

in mind that only a small proportion of my readers are surgeons and yet that all are interested in a general way in this subject. The field is a large one, any portion of which is worthy of high-powered study, but it will be looked upon on this occasion as a whole, and with but a very low lens.

First, it may be said without question that, as a result of this war, the treatment of wounds and infections has been advanced enormously and that this advancement must undoubtedly influence the practice of civil surgery.

Again, it may be said that the man who found himself in a position to carry out the treatment of wounds in the advanced hospitals, or even in the base hospitals alone, had at least an opportunity to learn a great deal and should benefit greatly from his military experience.

The men who served their country without being fortunate enough to do so in the field of their particular medical or surgical training and experience, the men who filled executive positions or acted as regimental surgeons, made much more of a sacrifice and deserve much more credit than those of us engaged in that line of medicine or surgery in which we were interested before the war and which we expect to follow now that the war is over. It is true then that he who made the greatest sacrifice is the one who will gain the least, from a professional point of view, by his experience.

As to the question of new antiseptics, there is not nor will there ever be an antiseptic that can supplant the aseptic treatment of wounds; that is, there is nothing we can use which alone will prevent a contaminated dirty wound, probably containing foreign bodies, from becoming an infected and suppurating wound. The war has definitely taught one great lesson in the prevention of wound infection, it is immediate and complete mechanical cleansing, what the French call débridement, what we might call mechanical antisepsis. It is difficult to find a single term to express just what this means; the word "excision" has been employed a great deal and Crile has made use of the term "revision," but neither, and certainly not the latter, is a comprehensive term. This mechanical cleansing is the most important step in wound treatment and the care with which it is carried out determines the proportion of wounds which may be immediately and completely closed and the proportion of infections and deaths from infections. Time and technic are the factors in the beginning. To close a wound immediately and completely it must be prepared for this closure with care and thoroughness; there must be the certain removal of all foreign materials and of all injured and contaminated tissue. Immediate débridement and complete primary suture without the use of chemical antiseptics constitutes the ideal treatment of a gunshot wound, and it is remarkable what results may be accomplished with care and experience. Before this war no one would have dared in

operating upon a gunshot wound to have closed the wound without a drain, and if he had done so there can be little doubt that a serious infection would have followed: and yet this is exactly what was being done in hundreds of cases every day during the last year or two of the war, not because of the employment of any germicidal agent, but through the practice of painstaking removal of everything in the wound which might infect it.

But there must of necessity be a large majority of wounds which cannot be immediately closed; the lapse of sufficient time for infection to occur between the receipt of the wound and the operation, say ten to fifteen hours, varying with the situation and character of the wound, the presence of comminuted bone and the necessity for immediate transportation, all render immediate suture unsafe. In order to render the ideal treatment possible, these wounds must be treated before contamination has produced an infection and the surgeon must be able to keep the patient under his immediate observation for at least two weeks. It is apparent then that it is during the so-called "quiet periods" that the best work can be accomplished; but even during the times of the greatest activity, with sufficient surgical teams, thorough débridement or mechanical cleansing can be accomplished and the closure of the wound may be done later when the patient has reached a hospital where he can remain until healing is complete.

One of the difficult things to give up was partial closure of wounds with the introduction of some form of drainage. Partial closure is an error, however, because it is much easier to sterilize and close a wound secondarily which has been left wide open than one which is partially closed with a drain. Hundreds of wounds were closed by what is called "retarded primary suture" within three or four days at a base hospital after an early débridement done nearer the front. Before this war, sterilization and closure of a large suppurating wound was rarely thought of and still more rarely practised, and yet this was the object of all treatment at the close of the war; and, moreover, it was accomplished in the large majority of cases.

Primarily the credit of successful wound sterilization is due to Carrel and Dakin, but certainly the surgeons in the American service owe much to Depage, Le Maistre, Duval and others who have elaborated or simplified the technic.

Here, again, just as in the primary operation, the success of the treatment depends upon the care with which it is carried out. Halfhearted effort only results in indifferent success. It was remarkable to see the different results obtained by different men and in different hospitals where exactly the same types of wounds were treated and supposedly the same method of treatment employed.

The most important factor in this sterilization is the thoroughness with which the primary operation is done, for if the surgeon should leave any foreign material, such as a piece of metal or a por-

tion of clothing, or even a portion of devitalized tissue, sterilization becomes difficult or impossible; and the second most important factor is the proper employment of the sterilizing agents. In the American hospitals where the best results were obtained the Carrel-Dakin treatment was employed. If this treatment was properly used, practically any wound free from foreign material was sterilized and closed.

The Carrel-Dakin treatment in infected wounds is one of the big things surgery has gained by the war, and the man who says there is nothing in it, that it is too cumbersome or that there are a number of other methods just as good, has either never seen a hospital where the treatment was being properly used or else he is so hide-bound that his opinion is worthless. I am afraid a number of American surgeons had this idea upon their arrival in France, but I am thankful to say that most of them became early converts to the method, and those who did not certainly were never able to produce results comparable to those obtained by the men who perfected themselves in the employment of the method. I never appreciated what this treatment was capable of accomplishing until I saw it properly employed in Carrel's own hospital at Compiègne, and then I was ashamed of my own wards. His wards contained scores of cases with large open wounds in the process of sterilization, and rarely was there a drop of pus to be seen. By adhering closely to the Carrel and Depage technic I am thankful to say we were able later in a number of our hospitals to duplicate their results.

I am not prepared to say that other agents, such as dichloramin-T, will not sterilize infected wounds, but I do think that there is no method so universally applicable and reliable as the Carrel-Dakin treatment, and this statement is not made on personal experience alone, but also on a fairly wide observation in many American, French and British hospitals.

There are two criteria for judging the germicidal power of any of these agents—the fall in the bacterial count, as shown in smears and cultures, and the ability to close the wound completely. No method that cannot stand these tests is worthy of consideration. In my opinion the bacteriologist is an absolutely essential factor in retarded primary and secondary closure of wounds, and I say this in spite of the fact that many surgeons became very expert in determining by clinical evidence only what wounds might be safely closed.

In no field of war surgery has the advance been so remarkable as in the treatment of gunshot wounds of joints. These wounds in our own Civil War were always treated by amputation or followed by severe infection, which frequently caused death or necessitated amputation. Up to the beginning of this war any surgeon who operated upon a gunshot wound of the knee-joint, for instance, and closed it without drainage would have rendered himself liable to a malpractice suit; and yet at the end of the war a surgeon who

did not close such a wound was open to the criticism of not doing up-to-date surgery. The results warrant the change in practice, for drainage invariably meant infection of a more or less serious nature and infection meant more or less incapacitating ankylosis or even worse. I have seen a straight series of ten gunshot wounds of the knee-joint, with fracture in all but one, treated by four surgeons (Pool, McWilliams, Jopson and Heuer) at Evacuation Hospital No. 1, heal by primary union and the patients leave the hospital with movable joints. And still can anyone doubt that surgery has advanced since and as a result of the war?

That these results can and must be obtained in civil practice is equally patent. Since my return to civil practice I have operated upon a pistol-shot wound of the knee-joint in which one ball perforated the head of the fibula, caused a gutter fracture of the condyle and a comminuted fracture of the patella, and another ball entered through the shaft of the fibula and perforated the head of the tibia. Early débridement was done in this case and the wounds closed without drainage. Primary healing took place and the man left the hospital within a few weeks with considerable motion in his knee-joint. I am sure that without my own military experience behind me, or that of others, this man would today still have discharging sinuses and probably a stiff knee-joint.

Another field in which the advance has only been secondary to that of joint surgery is in the treatment of gunshot wounds and infections of the chest. Nothing so much lowers the mortality rate and the percentage of infections in gunshot wounds of the chest as the early débridement and closure of the pleural cavity in all sucking wounds of the chest. Few of the cases of perforating wound, or small penetrating wound, where there was no sucking of air into the pleural cavity with each respiration, were subjected to operation unless subsequent infection of the hemothorax occurred, and in my experience it was surprising to see how small a proportion of the cases of hemothorax became infected. There was a definite practice in our own service that any wound of the chest that was operated upon should not be drained, but the wound completely closed. It must be admitted that a small percentage of these cases broke down or became infected later.

Probably the greatest improvement in the treatment of infections of the pleura we owe largely to Depage, who suggested and practised the sterilization of the pleural cavity by constant irrigation with Dakin's solution. Many of you are familiar with the findings of the Empyema Commission in our camps in this country, and the reading of these reports should be sufficient to convince any doubter of the efficacy of Dakin's solution as a sterilizing agent. If there is an area in the body in which infection is tenacious it is the pleural cavity. These infected cavities can be readily sterilized and the chest wall closed, or allowed to close, with absolute disregard of the

cavity itself. Tuffier and Depage have both shown, and hundreds of others have confirmed the observation, that if the cavity is sterile it will remain closed and the lung will expand. This, then, must be our practice in civil life in the treatment of empyema, and when one remembers the prolonged suppuration in these cases and the difficulty of obliterating the cavities by various plastic operations, one must admit that here again we are indebted to military surgery for a great advance.

Gas gangrene early in the war became a formidable enemy and continued so to the end. The gas bacillus was the *bête noir* of the surgeon; it was the cause of more amputations and more deaths than any other organism. Early and complete débridement was the surest means of avoiding the gas infections, but, as this was often impossible, gas gangrene remained prevalent up to the end of the war. Bull's serum was used quite extensively in some of our hospitals, and I believe in some cases it arrested the infection; but in others it had no effect, and in a few the reaction was so severe that it was thought to have hastened an inevitably fatal termination. I cannot speak of its efficiency as a prophylactic agent, though in the latter months of the war I believe it was used quite extensively in the French and British Armies.

An old enemy of the military surgeon, the tetanus bacillus, certainly cut no figure excepting in the early months of the war; that is to say, it was practically wiped out after the use of the prophylactic injections was regularly enforced. I consider it rather remarkable that during the nineteen months spent constantly in surgical work I saw only two cases of tetanus, and neither of these occurred, in the American service. In the early days of the war the French surgeons saw a good many cases of tetanus, but in recent years, with the prophylactic injections in every case of wound, it certainly became the rarest of all infections. One of the two cases I did see occurred in a poor Tommy who was brought into a British clearing station after fourteen days in No Man's Land, and he, of course, did not have the prophylactic injection. This was one of the most pathetic cases that I encountered, and it illustrates, if illustration is needed, that this has been a war in which, owing to the brutality of our enemy, chivalry and humanity were conspicuously absent. Such a thing as a temporary truce for the removal of the wounded was unheard of. This poor man, to whom I have just referred, in spite of an infected wound of the buttock containing clothing, dragged himself from one shell hole to another for fourteen days, living on the food and water which he found on the dead. The most pathetic feature of his case was the fact that although the infected wound of his buttock was being well taken care of and the infection well walled off, he succumbed the day after admission in the agony of tetanic convulsions.

Although we cannot say on reviewing our experiences what the

great Ambrose Paré said after recounting his achievements that "There is nothing left for posterity to discover," or of ourselves what Job said of his comforters, "No doubt that wisdom will die with you," yet there can be no doubt that surgery has made strides in certain directions, and that at least some good has come out of this great evil from which the world has suffered during the past four and a half years.

SOME CLINICAL MANIFESTATIONS OF INFLUENZA IN CHILDREN.[1]

By Linnaeus E. La Fétra, M.D.,

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The influenza epidemic of 1918, as it affected New York last fall, cannot be regarded otherwise than as a veritable plague. Nothing like it has been experienced by this generation. The poliomyelitis epidemic of 1916 seems almost insignificant by comparison. Previous epidemics of la grippe we have had ever since 1899, but nothing comparable to this scourge. The disease behaved so differently from any other epidemic that it seems difficult to believe it due to the same microörganism. The pathological findings, moreover, were in many ways very different from those found in other la grippe epidemics.

Two features especially stand out with regard to this epidemic: (1) The wide prevalence of the disease throughout all classes and ages, and (2) the great number and the exceedingly high mortality of the cases with pulmonary complications. Early in the epidemic it was frequently stated that infants and young children escaped the disease, but this was distinctly not true. It was true that the mortality among children was very low compared to that among young adults, and especially as compared to that among pregnant women. But children of all ages were striken with the disease, and, as will be shown later, pneumonia and bronchopneumonia were the common and often fatal complications in all the severe cases.

As to the wide prevalence of the disease among children, I may note that at Bellevue the Children's Medical Division has 140 beds; during the epidemic in October, November and December, 1918, our daily census rose to between 300 and 360, the rise all due to cases of what we must regard as influenza. At times we had as many as 60 admissions per day, and frequently several children of a family would all come in at one time. I recall distinctly one family of seven and another of eleven including adults, who came to the

[1] Read before the Section on Pediatrics, New York Academy of Medicine, March 13, 1919.

hospital on the same day, two ambulances being required to bring them all. At times the social workers or policeman on the block would find every person in the household or flat ill with the disease, no one being well enough to go out. In other instances the adults and older children would be ill, leaving no one to care for the smaller children, so we had many well children brought in along with the sick children and adults. Of course, separate provision had to be made for taking care of these well babies.

Physicians in the tenement districts reported there was barely a flat without the disease, whole families being stricken almost simultaneously. One doctor reported that he had made fifty calls in one block on one day, and that he had to refuse more for lack of time.

During the months of October, November and December, 1918, we treated in the Bellevue Children's Medical Division over 900 cases due to the epidemic. The great majority of these patients were not very sick, having only a moderate fever after the first day, with symptoms in the upper respiratory tract or pharynx. A large number had severe tracheitis. Only about 10 per cent. had pneumonia or bronchopneumonia, and of these about half proved fatal, the mortality being nearly all in the cases of bronchopneumonia. It was noted especially that when the children belonged to families in which the adults had pneumonia the cases were much more severe and liable to be fatal, so that in many instances whole families were entirely wiped out or only one or two of the younger children left. In this connection a possible explanation of the generally lower mortality among children is that the children are put to bed at once when they have a little fever or do not feel well. They therefore get the great advantage of bed rest from the outset. Older children and adults try to "fight the disease," so to speak, and, like walking cases of typhoid, these patients suffer more severely.

The cases met with may be divided into several main divisions:

1. *Those with High Fever and Prostration but without Physical Signs of any Localization.* These cases are often very puzzling, especially if the temperature continues more than two or three days. The fever is liable to vary widely between morning and evening, ranging from 100° in the morning to 103° or even as high as 106° in the afternoon; occasionally the temperature may fall to as low as 96° within a few hours. When the temperature is high the patients are badly prostrated, showing signs of general toxemia; but when the temperature is normal, or nearly so, they are bright, have a good appetite and digestion and seem hardly sick. Often after the first few days, even when the temperature is high, the child will show no evidences of the fever in the way of fretfulness, drowsiness or prostration.

2. *Cases with Rhinitis or Pharyngitis, or Both.* The greatest number of patients seen at Bellevue were of this type, numbering more than half the cases. The pharynx is red and glazed, often with

the lymph follicles on the posterior pharyngeal wall red and swollen. It is surprising how slight an amount of pharyngitis can apparently be the cause of high temperatures in young children and infants. This is so even without the presence of swollen tonsils. When the tonsils are swollen there is likely to be, after one or two days, swelling of the adjacent cervical glands, and the fever will persist until after the swelling, not only of the tonsils but of the cervical lymph nodes has entirely disappeared. Acute follicular tonsillitis alone was very seldom seen.

3. *Cases with Tracheitis and Laryngitis.* A very important group of patients were those that suffered from inflammation of the trachea or of the trachea and larynx. Tracheitis was far more frequent than laryngitis and was frequently combined either with rhinitis or with bronchitis. A characteristic symptom is the loud, barking cough which is almost incessant, and in younger children it is frequently so severe as to be accompanied or followed by spasm of the larynx. The crowing inspiration, together with the cough, frequently suggests whooping-cough, and is undoubtedly due to the same mechanical condition that produces the cough in that disease, namely, a mass of tenacious mucus at the lower part of the trache. Efforts to dislodge this by the cough are accompanied by contraction of the larynx, and often result in a cramp which is followed by the whoop of the next inspiration. Dr. Wollstein has shown by studies made at the Babies' Hospital some years ago that the influenza bacillus produces a severe tracheitis, resulting in just this form of spasmodic cough, frequently accompanied by a whoop. For these patients, of whom there were a large number, the most satisfactory treatment was to put them in a room in which there was a constant vapor of steam with creosote. To each quart of water in a croup kettle 30 drops of creosote were added, and this was kept boiling constantly. Dry air, either cold or warm, was found to aggravate the cough, and this was especially so if the dry air was cold.

4. *Cases with Bronchitis.* There is nothing peculiar about the bronchitis cases except that the smaller tubes are more liable to be involved, and there is commonly associated some inflammation of the upper respiratory tract, especially the trachea. Moreover, the severe cases are likely to develop into bronchopneumonia.

5. *Cases with Pneumonia.* Only about 10 per cent. of the cases had pneumonia. About four-fifths of the cases with lung involvement took the form of bronchopneumonia. This is in very strong contrast to what usually obtains in pneumonia in infants and children in whom the prevailing type in more than half the cases is lobar pneumonia.

The bronchopneumonia is peculiar in that the signs develop very slowly and irregularly except in those cases that are overwhelmed by the disease. Then both lungs, front and back, are filled with fine rales, especially the lower lobes behind. The consolidation is

patchy and the signs appear irregularly. Frequently the patches increase in size, so that they coalesce to involve the whole lobe. From the manner of development it is clear that the massive consolidation in these cases is due to confluence of the lobular pneumonia and is not a true lobar pneumonia. Commonly there are areas of dulness and bronchial breathing in two or more lobes, or else what indicates the same thing, patches of very fine rales in the midst of larger rales. Pleuritic crepitations are found in the bronchopneumonia of influenza far more often than in ordinary bronchopneumonia. Moreover, empyema occurred in five of the cases, an unusual complication in ordinary bronchopneumonia. The more frequent occurrence of pleurisy with its friction rales causes the signs of lung involvement to last for a longer period during convalescence than we usually find them.

Cyanosis was present in only the severest cases of capillary bronchitis and bronchopneumonia, but the spectrum of the blood failed to show methemoglobin in the only marked case we investigated. The occurrence of cyanosis is not frequent in children suffering from influenza pneumonia, in contrast to what prevails with adults.

The most peculiar feature of bronchopneumonia cases was the occurrence in six instances of interstitial emphysema. Appearing first above or below the clavicles it extended to the thorax, the arm and the back, in two cases down as far as the nipple and in one instance down the trunk and as far as the middle of the thigh, the crepitations being felt throughout the entire area. Apparently the symptom occurs in only the severest cases, for five out of the six died. One child, a boy, aged three years, seemed to be in good condition when the emphysema first appeared in the neck, and it was thought both from the few signs in the lung as well as in the heart action and from his good general condition that he would recover. However, the child succumbed on the third day. In the last case, the patient with double bronchopneumonia of rather chronic course, emphysema appeared all along the right side of the neck and thorax. By means of overlapping rubber adhesive straps, that side of the chest was put at rest and the emphysema gradually disappeared. This child recovered. Perhaps he would have survived without the strapping, but it seemed rational to prevent movement of that lung with further increase of the emphysema.

Just how this interstitial emphysema develops is an interesting and puzzling question. Either the air must pass into the cellular planes of the neck from the mediastinum through a rupture of the bronchi or air vesicles in that region or else it must pass through the adhesions of the two pleural layers, visceral and parietal, in the region of the apex; for in none of these cases was there air in the pleural cavity to form a pneumothorax.

I have asked Dr. Symmers, the chief pathologist at Bellevue,

about his findings at the autopsies, and he tells me that in only one instance was he able to determine the site where the rupture in the lung took place. In this case the air broke through the left lung near the mediastinum and then extended backward behind the pericardium into the cellular planes of the neck. In another instance it was probable that the rupture was in the region of the apex of the lung, but the exact site was not determined. In several cases a pneumothorax resulted from rupture of the visceral pleura and passage of air into the pleural cavity.

As sequelæ of the bronchopneumonia there is frequently some thickening of the bronchi or intra-alveolar infiltration as determined by the roentgen-ray plate. This leads to the radiographic diagnosis of pulmonary tuberculosis, but in two cases I have been able to follow, roentgen-ray plates taken after three months have shown a return to normal lung shadows.

In the matter of blood counts there are great variations. I have met some with a low leukocyte count, with low polynuclears and some cases with a high total and polynuclear count. The variation in the counts probably depends upon the complicating pharyngitis or bronchitis. It is not true that the influenza of children is characterized by a leukopenia, as that of adults seems to be.

The tachycardia that follows the disease has been noted by everyone who has followed the severe cases, and the older children require more care after an attack of influenza than the younger ones. This is because the small child has a large heart in comparison to the size of his body, and as he grows larger the heart gradually becomes smaller in proportion. Relaxation murmurs and excitable heart action may persist for a long time during convalescence.

The gastro-intestinal tract is seldom involved in the inflammation. In two cases, however, there was bloody dysentery, with much blood in the stools. The kidneys are not especially involved.

Very noteworthy in this epidemic as compared to former ones was the infrequency of otitis media and of influenza meningitis. Only a very small number of the patients, even those with marked involvement of the pharynx and tonsils, suffered sufficient inflammation of the middle ear to require paracentesis. In previous epidemics otitis was a very common complication. Absence of influenza meningitis was also very notable. In no instance was this condition found, although meningitis occurred in three cases. In all of these, however, the meningococcus was the causative organism.

TREATMENT. With regard to the treatment of influenza there is nothing specific to combat the disease directly. Even for prophylaxis, vaccines, from which so much was hoped and for which great claims were made, do not seem to have brought about results that are definitely advantageous. For the general treatment of the disease the most important thing is rest in bed from the very beginning until convalescence is well-established, the patient not

being allowed out of bed until after four or five days of normal afternoon temperature. In my experience the next most efficacious measure is the hot tub bath, repeated two or three times during the twenty-four hours. The temperature of the bath should be 2° or 3° below that of the patient, and the body should be thoroughly rubbed during a period of from five to ten minutes while the patient is in the tub.

For the catarrhal inflammations of the upper respiratory tract, and especially for the severe cough of tracheitis, for the laryngitis and for the spasmodic contraction of the bronchi, so frequently present in bronchitis, steam inhalations, with the addition of creosote are of the greatest help.

Patients with bronchopneumonia who have nasal obstruction or mouth breathing from dyspnea fare much better in an atmosphere of warm moist air than by the cold-air treatment. It is only after nasal breathing is easy and satisfactory, and after all spasmodic contractions are overcome, that the cold-air treatment is of benefit. For cases of lobar pneumonia without mouth breathing the cold-air treatment is of advantage from the outset. In all cases of capillary bronchitis and bronchopneumonia, and in many cases of lobar pneumonia, the early use of digitalis is of distinct advantage even if the administration is given for only twenty-four hours at the outset. This digitalization of the heart early in the disease permits of a more effective use of the digitalis later, should the need for it arise.

The course of the disease is very uncertain, and relapses and reinfections of different systems are not at all infrequent. It is therefore necessary to make careful examination of the throat, ears and lungs each time the patient is seen unless the temperature is absolutely normal.

PRIMARY CARCINOMA OF THE VERMIFORM APPENDIX: A REVIEW OF THE LITERATURE, WITH A REPORT OF TWO NEW CASES.

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(From the Clinical-pathological Laboratory of J. J. Coons, B.S., M.D., and H. M. Brundage, M.D.)

Before considering previous cases I desire to present the following case reports:

Case I.—*History.* Miss M. G., aged twenty-six years, was admitted to Mt. Carmel Hospital on May 22, 1917. Service of Dr. C. S. Hamilton.

Complaint. Attack of pain in the midabdomen two weeks previously.

Personal History. Negative except pain in the side. Tonsillectomy about four years ago. Menstrual history negative.

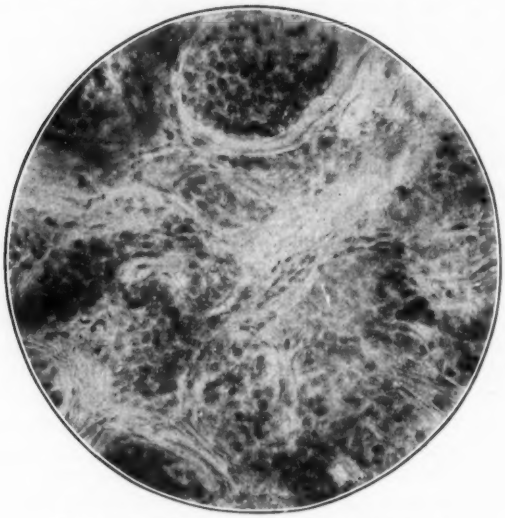

FIG. 1.—Case I. High-power photomicrograph.

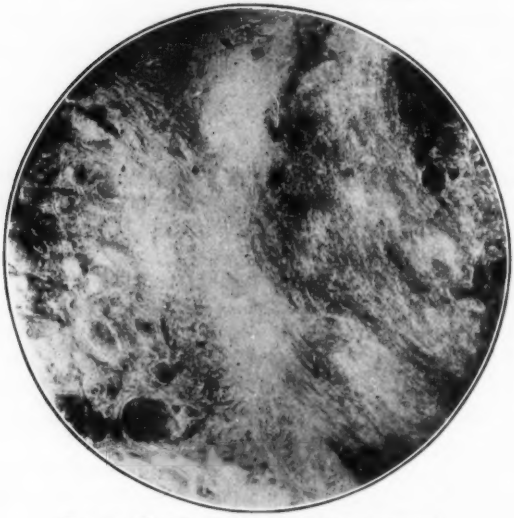

FIG. 2.—Case I. Low-power photomicrograph.

Present Illness. Has had attacks varying in frequency, several per year, for the last ten years. Has never been nauseated or vomited during any of these attacks, nor were the attacks severe enough to place patient in bed. Hypodermic injections were required to allay the pain. No movement of bowels during the attacks.

Physical Examination. Head and neck negative. Heart and lungs normal. Abdomen: no tenderness or discomfort at time of examination.

Operative. Incision rather high. Tremendous enteroptosis. Normal gall-bladder and kidney. Typical chronic appendix, reduced in size, irregular in shape and thickened, containing concretions. Appendectomy was performed. The patient made an uninterrupted recovery and left the hospital two weeks later.

Pathological Report. Gross appearance. The appendix is 5 cm. long, 7 mm. in diameter at the proximal third and 9 mm. through the distal portion. There are no adhesions and nothing suggestive of malignant growth. The lumen of the proximal portion is patent and contains fecal concretions. The lumen of the distal portion is obliterated by a fibrous growth. The wall of the distal portion is thickened to about 3 mm.

Microscopic Appearance. Section through the proximal portion shows the mucous membrane intact. The lymph nodes are slightly enlarged and the mucosa and submucosa are infiltrated with lymphoid cells. The muscular coats show a similar but less marked infiltration. There is no suppuration. The serosa is normal. The picture is one of a mild diffuse appendicitis.

Section through the distal portion exhibits an entirely different picture. The lumen is entirely obliterated by a mass of fibrous tissue. Scattered throughout this mass are numerous alveoli of epithelial cells. The alveoli vary in size and shape and contain from 4 to 200 or more cells. These cell nests show no apparent central degeneration or necrosis. Single epithelial cells are distributed diffusely and there is a slight infiltration of lymphoid cells. The mucous membrane is entirely absent. There is a submucosa, the fibrous nature of which is largely replaced by the epithelial cells of the new growth. No lymph nodes are seen. The muscular coats, especially the outer longitudinal layer, are infiltrated by a dense mass of epithelial cells, arranged singly and in alveoli. The new growth seems to have penetrated in all directions, but stopped short at the serosa. The epithelial cells throughout the entire section are of the spheroidal type. A few mitotic figures are found. It is impossible to locate the starting-point of the neoplasm.

Diagnosis. Spheroidal-cell carcinoma.

CASE II.—*History.* Miss N. H., aged thirty years, was admitted to Mt. Carmel Hospital on July 18, 1918. Service of Dr. C. S. Hamilton.

Complaint. Pain in the side for many years. Acute pain at the time of admission.

Personal History. Pain in side. Has had some form of pulmonary trouble.

Present Illness. Acute attack in November, 1917, and again at present time.

Operative. Tense, hard lump in appendix area. Had discharged pus through bowel. Incision evacuated about 2 ounces of pus near the lower end of the cecum. Abscess surrounded by omentum. This was gradually released and the cecum and abscess cavity lifted out. The open end of the appendix was found and inverted. The patient made an uninterrupted recovery and left the hospital nearly three weeks later.

Pathological Report. Gross appearance. The appendicular mass is in the shape of a very much flattened sphere and measures 2 x 2 x 1 cm. The peritoneal surface is covered with fat. The specimen does not resemble an appendix. On section one finds six small cyst-like areas, arranged in the form of a rosette, containing a mucoid substance.

Microscopic Appearance. The mucosa is not found. The submucosa and the muscular layers are present, but seem to have undergone atrophic degeneration. Scattered throughout these two layers are cyst spaces lined with tall columnar epithelium. The cysts contain mucoid materal. None of the cells of the lining epithelium are of the goblet type. A basement membrane appears to be present in some parts but absent in others. Three mitotic figures were found. The serosa is not involved.

Diagnosis. Columnar-cell adenocarcinoma.

Historical Review. A survey of the literature bearing on this subject will not be amiss, and from it we may draw some valuable conclusions. The earliest record of primary carcinoma of the appendix appeared in 1838.[1] A few more cases were reported up to the beginning of the present century.[2 3 4] Unfortunately, however, these cases were not described sufficiently to be of any great value in our study; in fact, many of them were not described histologically at all. Since the year 1900 nearly 300 cases have been reported, and it is from a study of these later reports that much can be gleaned concerning the condition.

Age. Contrary to the age at which malignant growths usually present themselves, primary carcinoma of the appendix occurs comparatively early in life. This was early recognized, and Moschcowitz[5] considered it most common at the age when acute appendi-

[1] Merling: Jour. de l'expér., 1838 (quoted from Kelly and Hurdon, Diseases of the Vermiform Appendix).

[2] Weir: Carcinoma of the Vermiform Appendix, New York Med. Record, 1893, xliv, 825.

[3] Stimson, L. A.: Cancer of the Appendix Vermiformis, Ann. Surg., 1896, xxiii, 186.

[4] Wright: Boston Med. and Surg. Jour., 1898, cxxxviii, 150.

[5] Primary Carcinoma of the Appendix, Ann. Surg., 1903, xxxvii, 891.

citis is most common. Baldauf[6] gives the ages ten to forty; McKenty[7] twenty to thirty; Dietrich[8] seventeen to forty as the most common time for this condition. The greatest age limit is reported by Rogg[9] as eighty-one years. The youngest case on record is that of a child, aged five years, reported by MacCarty and McGrath,[10] who also give the average age as thirty years. Obviously no age is immune, but it is quite evident that the most common appearance is between twenty and forty years of age.

Sex. Although cancer is more frequently observed among females, observers are not all agreed as to the relative distribution between the sexes of primary carcinoma of the appendix. Baldauf[11] thought it present to an equal extent in both sexes. McKenty[12] believed that about 70 per cent. of the cases were among females. MacCarty and McGrath,[13] at the Mayo Clinic, found that in a series of over 8000 appendectomies, 73 per cent. of the malignant growths occurred in females. These percentages were obtained from a large number of cases, many of which were laparotomies for other conditions. As will be shown later, primary carcinoma of the appendix is never suspected clinically and only the histological examination reveals the true nature of the lesion. Hundreds of appendices are removed during operations on other abdominal organs, and this probably accounts for the greater percentage of appendicular carcinomata found in females. If, on the other hand, primary carcinoma is a common sequel to appendicular inflammation (as will be considered further), then we would expect to find the carcinomata more frequently among males, because 60 to 70 per cent. of appendicitis cases are males. This question may be settled best after more cases have been reported.

Frequency. Of all the cases of appendectomy very few reveal primary malignancy. Many cases were probably overlooked in the past. But now that microscopic examination has become a routine procedure more cases are coming to light. All investigators are agreed that less than 1 per cent. of appendicular lesions are of primary malignancy. Of 8039 cases at the Mayo Clinic,[14] 40, or 0.49 per cent., were primary carcinoma. Of 1700 cases examined in this laboratory, 4, or 0.23 per cent., were found to be primary carcinoma.[15] Of 300 cases observed at the Protestant Hospital no malignancy was found.[16] Of 13,151 cases reported by Reimann,[17] 17, or 0.13 per cent., were carcinomatous.

[6] Primary Carcinoma of the Vermiform Appendix, New York Med. Record, 1906, lxix, 716.

[7] On Appendix Tumor, Ann. Surg., 1912, lvi, 419.

[8] Deutsch. med. Wchnschr., Berlin, 1910, xxxvi, 13.

[9] Carcinoma und Carcinoid det Appendix, Ztschr. f. Krebsforsch, 1913, xiii, 12.

[10] Frequency of Carcinoma of the Appendix, Ann. Surg., 1914, lix, 675.

[11] Loc. cit. [12] Loc. cit. [13] Loc. cit. [14] Loc. cit.

[15] Coons, J. J.: Primary Carcinoma of the Appendix, Surg., Gynec. and Obst., 1908, vii, 5. [16] Scott, E.: Personal communication.

[17] Primary Carcinoma of the Vermiform Appendix, Am. Jour. Med. Sc., 1918, clvi, 190.

Clinical Diagnosis. Authorities are agreed that primary carcinoma of the appendix is very closely associated with inflammation of that organ, and in general, therefore, the symptoms of the former are those of the latter condition. Even if the neoplasm grows to a size larger than is usual it is still difficult to diagnose. Hurdon[18] efficiently discusses the matter by saying that the diagnosis is difficult, due to the absence of early distinctive symptoms; that there are no digestive disturbances manifest until the growth has invaded the cecum or intestine; and, furthermore, the condition may easily be mistaken for a cyst, calculus, neoplastic form of tuberculosis or a fecal impaction. It is of interest to note that several specimens have been removed postmortem as well as during operations for other conditions, where there was absolutely (?) no history of appendicitis. Thus, Mosse and Daunic[19] found carcinoma involving the whole length of the appendix in a woman who died from heart disease, with no history of appendicitis. Similar findings were obtained by Whipham,[20] Grünbaum[21] and others.

Etiology. Although the cause of cancer is still obscure, yet there have been some interesting theories stated concerning the etiology of primary carcinoma of the appendix. As stated above the condition seems closely related to inflammation, especially of the chronic obliterative type.[22] Kennedy[23] suggested that the new growth originated from the disturbance and separation of the epithelial cells of the mucosa. Lubarsch[24] believed that the cells lining the crypts of Lieberkühn were the mother cells of the growth. McKenty[25] believed that the condition was due, in part at least, to irritation, and its effect upon embryonic remains in the appendix. Other writers claim that displaced cells are liable to occur in the appendix, because it is either an involution structure or else an organ undergoing evolution, not far removed from the embryonic state. Many observers consider that the condition is secondary to inflammation, and, on the other hand, it has been claimed that the accompanying inflammation is secondary to the neoplasm. The former idea is probably nearer correct, because the condition is most frequently associated with chronic obliterative appendicitis. But neither of these two latter theories are at all satisfactory, since they explain neither the method by which the new growth begins

[18] Primary Carcinoma of the Appendix Vermiformis, Bull. Johns Hopkins Hosp., 1900, ii, 175.

[19] Bull. de la Soc. anat. de Paris, 1897, lxxii, 814.

[20] Primary Carcinoma of the Vermiform Appendix, Lancet, 1901, i, 319.

[21] Ein neuer Fall von primären Krebs der Appendix, Berl. klin. Wchnschr., 1907, xliv, 984.

[22] Elting, A. W.: Primary Carcinoma of the Vermiform Appendix, Ann. Surg., 1903, xxxvii, 549.

[23] Primary Carcinoma of the Appendix Vermiformis, Lancet, December, 1910, xvii, 1757.

[24] Schwartz: Tr. New York Acad. Med., April, 1913.

[25] Loc. cit.

nor the types and positions of cells which first proliferate. The question will be answered best after we know more about the etiology of malignant tumors and after further detailed study of primary carcinoma of the appendix.

Pathology. Gross appearance. Many of the earlier cases reported were not described. Many of the later cases, however, are depicted as typical chronic appendicitis, and most of these are of the obliterative type. Tumor formation is sometimes suggested by a small enlargement which seldom reaches a size greater than a pea, this occurring generally at the tip of the organ. But there is nothing distinctive in this swelling of the distal extremity. The writer has observed similar enlargements in many appendices which were entirely free from carcinoma. The new growth is by no means limited to the tip. Thus, Mosse and Daunic[26] report a case in which the carcinoma involved the entire length of the appendix. Kelly[27] found the new growth at the base of the organ, and a few other writers have reported similar findings. Adhesions may or may not be present; in fact, the tumor may be present in any condition of appendicular inflammation.

Microscopic Appearance. In the great majority of cases the new growth is confined to the mucous and submucous coats, with perhaps a slight tendency to infiltrate the muscular layers. A few cases, however, show infiltration of the muscular coats, but in nearly all of these cases the serosa is the limit of growth. An interesting exception is reported by Brandt,[28] who had a case in which the appendix was perforated by carcinomatous growth. Ross[29] had a case in which the mucous coat was entirely free from the tumor cells. The type of epithelial cell is not constant in all cases. The spheroidal cell is most common, but cuboidal, cylindrical, endothelial and mixed types have been found. The glandular type, so frequently found in intestinal carcinomata, is seldom found in the appendix. Mitotic figures are not numerous, but may be found by careful search. Occasionally, the cells may show mucoid degeneration, the so-called colloid cancer. Lymphoid-cell infiltration is common. Hertzler[30] points out that cancer of the appendix differs from the ordinary malignant types in that it lacks the usual round-cell infiltration; furthermore, that the connective tissue retains its acidophilic properties (these being lost in malignancy).

Malignancy and Metastasis. Perhaps the most interesting feature is the generally benign nature of the condition. Some writers deny cancer, believing the tumor to represent endothelial proliferation as a result of inflammation or displaced epithelial cells following

[26] Loc. cit.

[27] Tumors of the Vermiform Appendix, Proc. Path. Soc. of Philadelphia, 1900, new series, iii, 109.

[28] München. med. Wchnschr., September 3, 1907.

[29] Carcinoma of the Appendix, Tr. Philadelphia Acad. Surg., 1912, xiv, 90.

[30] Treatise on Tumors, 1912, p. 505. Philadelphia, Lea & Febiger.

suppuration.[31] Oberdorf suggested the term "cancroid," believing that the neoplasm was not a true cancer but merely resembling it. Clinical evidence generally bears out this idea, but pathologically it is extremely difficult to exclude true carcinoma in every case, especially those diagnosed as adenocarcinoma. Although there is no marked tendency toward metastasis, yet we have several records of metastatic growths. Whipham[32] reported a case with secondary involvements in the liver, ovary, lymph nodes and peritoneum. Le Conte[33] had a case with metastasis to the cecum. Brunton and Glover[34] reported a case of carcinoma of the distal end, with adhesions to the iliac fossa, recurrence of the condition resulting fatally. The new growth may cause perforation leading to peritonitis. According to Kelly and Hurdon[35] the regional lymph nodes are involved only late in the disease.

The author is indebted to Dr. E. Scott and Miss Cameron, of the Ohio State University, for their kind assistance in producing the photomicrographs.

HUMAN ANTHRAX.

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The following report of a case of human anthrax involving the neck is made because of some unusual and interesting features. The anthrax bacillus was not only recovered locally from the lesion, but was also found in the patient's shaving brush. Anti-anthrax serum was employed exclusively in the treatment, given both by intramuscular injection and locally by injection into the tissues immediately surrounding the malignant pustule. The latter method of treatment proved exceedingly effective, and since we have been unable to find any record of serum previously having been used in this way in the therapy of anthrax, it seemed advisable to report the case in detail. Excision of the lesion proved entirely unnecessary after the local application of the serum.

Case Report. R. T., aged twenty-six years, was admitted to Kingston Avenue Hospital, November 21, as a case of parotitis.

[31] Ross: Loc. cit. [32] Loc. cit. [33] Proc. Am. Surg. Assn., 1908.
[34] Brunton, T. L., and Glover, L. G.: Malignant Disease of the Appendix Vermiformis, Lancet, February 12, 1910, p. 419.
[35] The Vermiform Appendix and its Diseases, 1905, p. 743.

Family History. Family history negative.

Previous History. Had measles, pertussis and parotitis when a child. No disease during adult life.

Present Illness. On Monday, November 18, while shaving the patient accidentally cut himself on the right side of the neck. The wound bled a little, but he paid no attention to it, lathering soap over the cut surface with a new shaving brush which he had just purchased and which previous to use he had washed and placed in some boiling water. On the following day, about noon, the patient began to feel sickly, complaining of headache, backache and generalized pains all over the body. Toward evening the same day his neck became rather stiff, especially on the right side, so that it hurt him to turn his head around. This he attributed to a small pustule which had developed in the place in which he cut himself. During the night he experienced a slight chill and felt somewhat feverish. He noticed particularly that his eyes pained him so that it was impossible to read. On awakening the next day, on November 20, the swelling of the neck had become more marked and painful to touch, and he felt as if it were exerting an inward pressure, but not sufficiently as to interfere with respiration or deglutition. He also noted that his voice was slightly husky.

Clinical Course. The patient was sent into the hospital as a case of parotitis and no special notice seemed to have been taken of the pustule on his neck at the time.

November 23. Patient came under the observation of one of the writers. Physical examination at this time gave the following findings: Patient presents the aspect of a person acutely ill, but without any marked prostration. He answers questions clearly and intelligently, but his voice is quite hoarse. Throat is congested; there is no exudate on the tonsils and no enlargement. The lungs are normal except over the right interscapular region, where there are a few moist rales, with inspiration. The cardiac sounds are of good quality. The abdomen is negative; neither the liver nor spleen are palpable.

On the right side of the neck, on a line with the anterior border of the sterno-cleido-mastoid muscle, and about one and a half inches below the angle of the jaw, there is considerable swelling. The center of the swelling is occupied by an elevated pustule, measuring about 25 mm. in diameter, resembling a large vaccination lesion about the ninth day. In the center of the pustule is a black, depressed eschar, and around this there is a white elevated border, the so-called "blanched zone," which is about 3 mm. in diameter, and which in turn is encircled by a red areola. At the outer margin of the eschar there are a number of small elevations, resembling vesicles which discharge continuously a serous secretion. The tissues around the pustule are very edematous and infiltrated, the swelling extending upward to the angle of the jaw and backward

to the anterior border of the trapezius muscle. This edematous area is rather sensitive to pressure, but it does not pit and is not of a hard consistency.

Owing to the suspicious character of the pustule, smears and cultures were taken from the red indolent ulcerative surface by lifting up the margin of the eschar.

November 24. As the smears and cultures of the previous day seemed suspicious of anthrax, smears and cultures were again taken, the latter in nutrient broth and on several Petri dishes of blood-agar. A specimen of blood was taken for cultural purposes. At 10 A.M. 48 c.c. of anthrax serum were injected intramuscular in the right buttock. In the evening 10 c.c. of serum were injected into the indurated tissues immediately around the pustule. From 99° at 8 A.M. the temperature rose to 101° at 8 P.M. By 8 A.M. the following morning the temperature had fallen to 99° again. Evidently the febrile excursion was part of a serum reaction.

November 25. The patient's general condition remained good, but he was drowsy. There was considerable acute tenderness and a slight extension of the edema in the region of the pustule, and the lesion seemed more definitely elevated above the surrounding tissues. Another injection of 30 c.c. of anthrax serum into the right buttock and 10 c.c. of serum into the region around the lesion were given.

November 26. The inflammation and swelling around the lesion were quite marked in the early part of the day, but subsided rapidly by evening, leaving the indurated tissues about the pustule somewhat reduced in size.

November 27. The pustule has now shrunken considerably and has lost its red areola, but it stands out more prominently from the underlying tissues, owing to the fact that the induration of the surrounding tissues is much less. The most marked swelling is now localized to a mass of glands situated just below the angle of the jaw. Twelve cubic centimeters of serum were injected into the immediate region of these enlarged glands.

November 29. Another intramuscular injection of 30 c.c. of serum was given. Glandular swelling subsided rapidly.

November 30. Patient continues to improve clinically. Is somewhat drowsy after serum. The pustule is subsiding rapidly, apparently melting away.

December 2. Progress continues satisfactorily. There is slight soreness and swelling around the area of swollen glands in which the serum was injected. The lesion is now only a raw ulcerated surface even with the adjacent skin. Patient has several rather superficial abscesses scattered over the body. Incision and drainage of one on forearm. Cultures were taken.

December 12. Patient has lost quite a little weight since admission, but he feels well and has been up and around for the past

week. The lesion has now dried up, leaving a thick and very adherent crust, resembling in every respect a piece of burnt leather. This crust was removed, but only with great difficulty, as it was extremely adherent, and cultures were taken from its under surface, from the ulcerated raw surfaces beneath and from the seropurulent discharge which could be pressed from the lower part of the pustule.

December 14. Today the crust has reformed at the lower part of the wound. The rest of the lesion is even and smooth with the skin, not unlike a vaccination scar, but not so much depressed below the surface. A serous discharge was pressed from the lower margin of the wound after the crust was removed. This was cultured. Tincture of iodin was used locally to dry the pustule.

December 18. Patient feeling very well and lesion healed.

December 20. Discharged, apparently cured.

February 15, 1919. Patient again seen and examined. His health is excellent and there are no evidences of any detrimental effect of his recent attack of anthrax. At the site of the local lesion there remains nothing but a small circular scar, about the size of a dime, a little depressed below the surrounding skin.

Pathological and Bacteriological Findings. Blood Culture. Taken November 24, remained sterile. Evidently there was no blood infection.

Blood Counts. December 2. Total leukocytes, 19,600; polynuclears, 78 per cent: lymphocytes, 22 per cent.

December 4. Total leukocytes, 13,300; polynuclears, 72 per cent.; lymphocytes, 26 per cent.; eosinophiles, 2 per cent.; total erythrocytes, 5,680,000.

Urine Examination. November 25. Albumin, very faint trace; Fehling's, negative; reaction acid; specific gravity, 1030; occasional hyalin and granular cast. Culture and smears were made from centrifuged specimen, but the bacteriological examination was negative.

Smears and Cultures from Pustules. November 23. Direct smears showed pus cells, staphylococci and a fair number of bacilli; Gram-positive; long, square end and rough in outline.

Culture on agar plate in twenty-four hours showed many opaque grayish-yellow colonies, 1 to 2 mm., several 4 to 5 mm. dry, opaque, white, with scalloped borders. Microscopically the small colonies proved to be staphylococci; the large colonies were found to be composed of Gram-positive bacilli; large, square end, single and in chains. A handing drop showed the bacilli to be non-motile.

Large anthrax colonies transplanted to plain agar for further study.

November 24. Broth culture: The broth is cloudy. Examination microscopically shows numerous staphylococci and a few larger Gram-positive bacilli square end and non-motile.

November 25. Transplant colonies on plain agar have now

developed. They are dry, opaque and have fringing projections. On low magnification these colonies seem to resemble a head of hair. Smears from the colonies show the same large Gram-positive bacillus previously found. It is non-motile after several days. Other smears contained long chains of bacilli, showing spores of an elliptical shape, one in each bacilli.

November 24. Six more smears made from the pustule, stained by Gram and examined, showed pus cells, numerous staphylococci and a Gram-positive bacillus. Three more agar plates were inoculated from the pustule.

November 25. First plate: Colonies—many opaque, white, 1 to 2 mm. and some large, flat, opaque, dry, with fringes from the borders. Low magnification shows Medusa-head appearance, so typical of anthrax. Second and third plate showed same appearance.

Microscopic examination of smears from all three plates showed numerous staphylococci and many large Gram-positive square-end bacilli, single and in chain formation; non-motile.

Transplants made to broth, and the following day examination showed a dense sediment at the bottom of the tube, with the supernatant fluid clear. Hanging drop shows a non-motile bacillus.

Transplants made to gelatin, and examination made the following day showed white opaque colonies; at the end of two days the gelatin was completely liquefied.

Transplants made to agar for animal inoculation. In making transplants, material was taken from the fringes and was found to be pure. In one or two instances staphylococci colonies were found in the center of the large anthrax colonies, but the anthrax grew pure at the border.

Animal Inoculation from Cultures of the Pustules. Mouse No. 1. November 27, 7 P.M. An emulsion was made in broth of the pure growth obtained on agar. Then 10 drops of this emulsion were injected into the mouse at the root of the tail, the area of injection being sterilized by alcohol. The animal was in fair condition until 10 A.M. the following day, when it suddenly died.

Necropsy. At the point of inoculation there is an indurated and rather edematous area. On incision this induration is found to be composed of a glairy and rather gelatinous exudate. The neighboring lymph glands are enlarged and ecchymotic. No change was visible microscopically in the internal organs. Cultures were made on plain agar plates from the heart, liver, kidneys and spleen.

November 29. Cultures from the internal organs of the mouse were examined.

Liver: Many colonies +++; dry, white and opaque. Microscopic examination shows anthrax bacilli; non-motile.

Heart Blood: Many colonies ++++; dry, white and opaque, as above. Microscopic: Anthrax bacilli.

Kidney: Colonies ++++, same appearance. Microscopic examination shows anthrax bacilli.

Point of Inoculation: Gelatinous exudate; colonies ++++; same appearance.

The plates from these organs were kept for several days and preserved the appearance of anthrax colonies. The bacilli exhibited spore formation and a capsule was definitely demonstrated.

Cultures from the Shaving Brush of the Patient. The patient used the brush for the first time when he cut himself in the spot in which the pustule subsequently developed.

November 25. Agar plate shows many opaque, moist small to large-sized colonies Also a few large, dry, flat opaque-like anthrax. Microscopic examination of smears from these colonies showed many cocci, both Gram-positive and negative Many bacilli, short and long, some thick and some slender Some of the bacilli resembled those obtained from the pustule Transplants were made from the large, dry, flat colonies for further study.

November 26. Subcultures show colonies of one type, namely, dry, flat, opaque, with fringing borders. On low magnification these are thick and white, the fringes being more transparent.

Microscopic examination of smears made from the colonies show them to be composed of Gram-positive bacilli, long, thick, square end, single or in chains, and non-motile After several days spores appeared in the filaments.

Transplants made to broth and gelatin from the subculture on agar plates.

Broth: After one day a sediment appeared in the bottom of the tube. The supernatant fluid was clear.

Gelatin: White colonies appeared and in two days the gelatin was completely liquefied. The appearance of the colonies is identical with those from the pustule, and liquefaction proceeds at the same rate.

There are then no differences to be observed between the organism from the pustule and that from the brush as to colonies, microscopic appearance, spore formation and motility. It now remained only to inoculate a mouse to prove them identical.

Animal Inoculation on Mouse No. 2. December 2. The mouse was inoculated with an emulsion of anthrax colonies obtained from cultures of the shaving brush. About 10 minims of the emulsion were injected at the root of the tail. The mouse was fairly well for about ten hours, and then died suddenly.

Necropsy. Soft swelling at the point of inoculation. Internal organs seemed normal macroscopically except the spleen, which was enlarged. Direct smears and cultures were taken from the heart, lungs, liver, kidney, spleen and gelatinous edema.

Examination of Smears. In all there was found many anthrax bacilli. A fair number of the bacilli had a capsule. The form was often quite irregular. The ends frequently appeared bent like a hook. A few spores were present in the bacilli from the gelatinous edema.

Cultures. The growths on most of the plates, as those from the heart, liver and kidney, were pure anthrax, but on some of them there was also a slimy growth which proved to be a small Gram-negative bacillus, evidently a contamination from the skin of the mouse (normally a small Gram-negative bacillus lives as a saprophyte in the skin of the animal).

Subsequent Smears and Cultures from Pustule. December 4. A plate culture on agar was taken from the lesion. It showed only staphylococci.

December 14 Two other plate cultures on agar showed only staphylococci. Direct smears from the lesions showed pus cells and staphylococci.

December 4. Cultures from abscesses on the arm showed staphylococci.

RESUMÉ. 1. The definite history of the manner in which the disease was contracted—accidental cut during shaving and the use of an infected shaving brush.

2. The mildness of the attack, despite the situation of the malignant pustule in the neck.

3. The subsidence of the local and constitutional symptoms without excision of the lesion.

4. The apparent benefit of the intramuscular injection of anthrax serum.

5. The definite improvement in the pustule itself following the injection of anthrax serum into the indurated tissues of the neck surrounding the lesion. This local use of serum we believe is one of the prime essentials for the successful treatment of anthrax.

6. The absence of a blood invasion.

7. The recovery of the anthrax bacillus on several different occasions from the pustule, both by smears and cultures.

8. The absolute proof of its identity as anthrax by its morphology, its cultural characteristics, the effect in producing death on inoculation of cultures into mice and finally the recovery of the bacillus in pure culture from the animal. (The morphology of the organism in smears from the pustule is not enough to identify it. Its lack of motility and the fact that it possesses a capsule must be proved to differentiate it from the Bacillus subtilis and the bacillus of malignant edema.)

9. The recovery of the organism from the shaving brush of the patient. The similarity of this bacillus in its morphology, cultural characteristics and results upon animal inoculation to that which was found in the malignant pustule.

The writers take this opportunity to thank Mrs. B. Riehl, of the Laboratory Staff of the Hospital, for her valuable assistance in connection with the laboratory work upon the case.

THE METHOD OF OBTAINING CEREBROSPINAL FLUID BY PUNCTURE OF THE CISTERNA MAGNA (CISTERN PUNCTURE).

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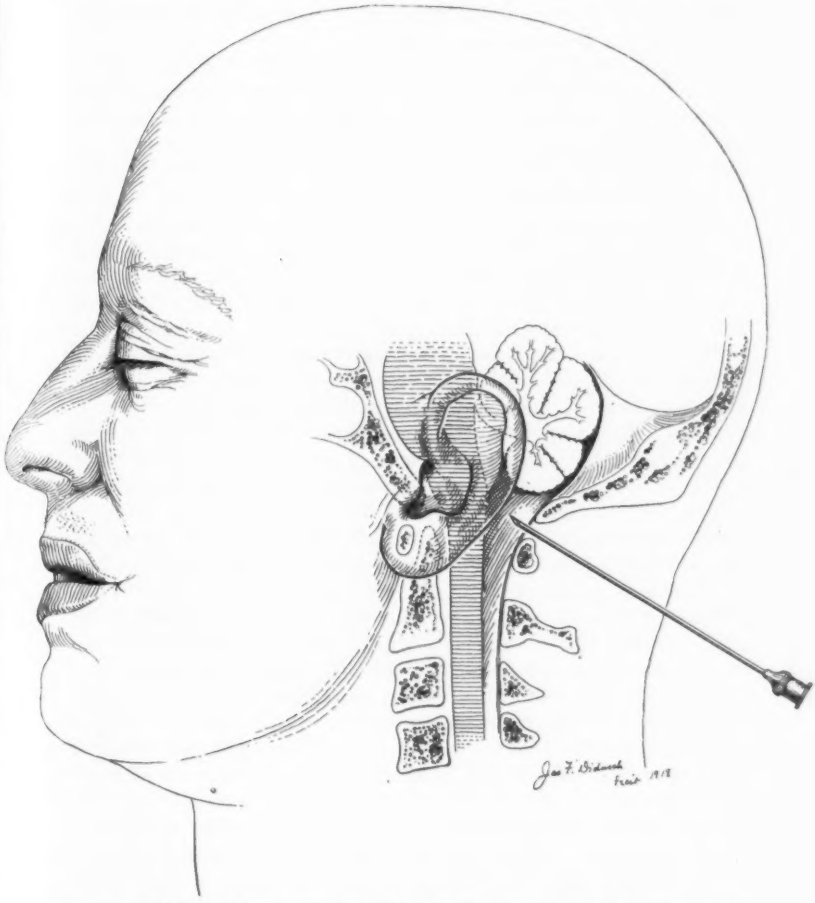
In conducting the early experiments on the physiology and chemistry of the cerebrospinal fluid, two routes for securing the fluid from animals were employed. The first of these was the lumbar and the other was that afforded by the space between the occipital bone and the first cervical vertebra, a position which recommended itself, since at this point no bony obstruction interferes with the approach to the subarachnoid space, the opening here being covered by the occipito-atlantoid ligament. Both routes were utilized, however, only after a preliminary operation was performed; in the lumbar region the spinal membranes were exposed by laminectomy, and in the cervical position the ligament was bared by a median incision through the structures of the back of the neck. Such procedures, while they served their purpose well for acute experiments, made it difficult to conduct observations over a prolonged period. In 1890 Quincke demonstrated that the lumbar fluid spaces could be reached by direct puncture, and so placed in the hands of clinicians a valuable method for obtaining human spinal fluid for analysis. Unfortunately the ease of withdrawing lumbar spinal fluid in man does not apply to laboratory animals when the intervertebral spaces are narrow and very oblique. Because of this anatomical arrangement, experimentalists continued for some time, subsequent to Quincke's demonstration, to experience difficulties in securing specimens for study without resorting to the annoying feature of preliminary operation. Dixon and Halliburton,[6] in 1913, showed that the cerebrospinal fluid reservoirs of a dog could be reached successfully by a direct puncture through the occipito-atlantoid ligament. This method has since been used extensively by Weed,[14] and in the Army Neurosurgical Laboratory, under his direction, it has been relied upon almost entirely for the exploration of the subarachnoid space.

The technic for performing occipito-atlantoid puncture in animals is quite simple, and, after a little practice, not much difficulty is encountered in securing perfectly clear normal fluid. To locate the

occipito-atlantoid ligament in the cat the thumb is placed in the depression situated below the occipital protuberance and limited laterally by the superior nuchal lines. By manipulation of the head a definite soft spot may be felt at the lowest part of this depression, just above the spine of the axis. This area corresponds to the interruption in bony continuity between the base of the skull and the spine. The fluid reservoir lying just below the ligament constitutes the lower part of the cisterna cerebellomedullaris, and it has at this level in the cat a depth of about 5 mm., representing the distance between the inner surface of the ligament and the posterior surface of the cord. The nervous structures at the level of the ligament constitute the transition between the spinal cord and the medulla, so that care must be taken not to advance the needle too far in performing the puncture. The space afforded by the cistern is quite sufficient, even in such small laboratory animals as the rabbit, guinea-pig and even the rat, to permit repeated punctures in this area without causing injury to the nervous tissue. Observance of the following points in technic have been of service in performing the operation in this laboratory. The instrument found to be most satisfactory is an 18-gauge lumbar puncture needle cut down to about 5 cm. The point must be sharp, but the bevel should not exceed 2 mm. The skin is pierced in the midline just above the spine of the axis, but before proceeding further the subcutaneous tissue should be freed from the point of the needle to prevent its deflection during the next steps of the procedure. The head of the animal is then firmly grasped in the left hand, the thumb resting in the depression below the occipital protuberance. Using the left thumb as a guide, and with the head well flexed, the needle is carried carefully into the cistern. The direction must be slightly upward rather than perpendicular to the skin, so that the needle will be directed obliquely to the cord and medulla and further advance will carry it higher into the cistern rather than into the nervous structures. As soon as resistance ceases to be felt the operation is complete and removal of the obturator should be followed by the appearance of cerebrospinal fluid. Sometimes on removing the obturator, however, pure blood will issue from the needle. In such cases it will be found that the puncture has been made too near the edge of the ligament, and one of the suboccipital veins in the neighborhood has been entered. Usually in such cases the needle has not entered the subarachnoid space and a second attempt with a fresh instrument will yield clear fluid.

An analysis of 1186 punctures of the occipito-atlantoid ligament done on cats in this laboratory showed that an injury of the medulla was occasioned only ten times (0.84 per cent.). By a further analysis of these figures it was found that seven of the accidents occurred during the early months of the work, and among the last 527 punctures similar injuries were made only three times. Several

of these were brought about by attempts to obtain fluid for analysis from animals which had been given a purulent meningitis. In these early experiments it was not realized how very thick and viscid the spinal fluid could become in a cat, and when a flow did not follow



Topographical study to show the landmarks used in performing cistern puncture. Composite prepared from numerous tracings of frozen sections. One-half actual size.

the removal of the obturator from the needle the technic was blamed and further prodding in the attempt to locate a pocket of fluid would end occasionally by injury of the medulla. When puncture has been properly performed and no fluid obtained it was subse-

quently found in thirty-five dry taps that failure was due to lack of fluid, increase in its viscosity or to adhesions, and not to faulty technic. Consequently, in later experiments such cases were not further explored. The presence of a small amount of blood cannot be avoided in all cases, but of the fluids obtained 69 per cent. were free from red elements, a proportion which could be greatly increased by considering the recent cases only.

The method has proved so satisfactory in the laboratory and so safe in experienced hands that it was thought advisable to investigate the possibility of its use clinically. Accordingly, investigations were undertaken on cadavers with the object of determining the anatomical relations in the human subject. The accompanying drawing is a composite made from numerous studies of frozen head sections and represents the relations of the structures to be considered in the average subject. The occipito-atlantoid ligament stretches from the posterior rim of the foramen magnum to the corresponding position on the first cervical vertebra. Closely applied to its anterior surface is the dura mater and directly under this meninx lies that portion of the arachnoid membrane which forms part of the posterior wall of the cisterna cerebellomedullaris. The anterior wall of the cistern is formed by the posterior surfaces of the upper cervical cord and the lower part of the medulla. The depth of the fluid reservoir, namely, the distance between the arachnoid and the posterior surfaces of the cord and medulla, is about 1.5 cm. at the level of the occipito-atlantoid ligament. For introducing the needle a point is selected in the midline of the back of the neck just above the spine of the axis. The glabella and the upper edge of the external auditory meatus were found to be valuable structures for directing the course of the needle, for a plane passed through them and the point of insertion on the back of the neck will pass also through the occipito-atlantoid ligament. This relationship has been a constant one in all of the subjects studied and is clearly shown in the illustration. In thin individuals palpation over the back of the neck often reveals a deep depression between the occipital protuberance and the spine of the axis, and with the tip of the finger the approximate position of the occipito-atlantoid ligament can be directly located. The distance necessary to insert the needle in order to reach the cistern varies, of course, with the individual. From a number of measurements taken at the time of puncture on cadavers the average distance was found to be 4 cm., and it rarely exceeded 5 cm. or was less than 3 cm. In view of the uncertainty occasioned by such measurement the operator will find it necessary to rely upon his tactile impressions produced when the point of the needle overcomes the resistance offered by the ligament and dura and passes into the cavity of the cistern. For one skilled in performing lumbar punctures this sensation is quite definite, and for us, in performing the operation both in the clinic and at autopsy, it has given an

infallible index of when the cistern has been reached. After punctures on the cadaver the needle was left in place in several instances and the brain was removed. In this way an idea was obtained concerning the exact position the point of the needle assumed and how far it actually projected into the cistern. Such controls showed that the needle never projected far enough to cause any great anxiety that the medulla would be injured if the operation were carried out in experienced hands. Furthermore, it was learned that the skull could be moved on the occipito-atlantoid articulation in all directions without appreciably altering the relations of the needle point to the nervous structures. These tests were made, for it was felt that the relations between the posterior wall of the cistern and the medulla might be so altered as to cause damage to the nervous system were a patient to give a sudden unexpected movement of the head while the needle was *in situ;* the findings indicate that such movements of the head when the needle is in place would not be dangerous.

When once we had become familiar with the technic it was found that on cadavers the operation was easier than lumbar puncture and that fluid was more readily obtained at this point. It has therefore become our routine practice at the autopsy table, where examination of the cerebrospinal fluid is required, to obtain it by cistern puncture. This, then, is offered as our first use of the method.

In the living, one of the first uses to which this method recommends itself is in cases of spinal subarachnoid block incident to the course of meningitis. The presence of such blocks is manifested usually by the inability of the physician to obtain spinal fluid in the lumbar region, and the occurrence has led, in a number of instances, to the utilization of other routes for reaching the fluid reservoirs. Such complications led Chartier[4] to make the puncture in the eighth dorsal space in two instances, and later a case similar to his induced Ravaut and Krolunitsky[13] to insert the needle between the sixth and seventh cervical vertebræ. Both of these routes were used successfully by Netter.[11] Quincke[12] early suggested that fluid could be obtained from the cisterns by suitable punctures, but considered them impracticable and dangerous for routine practice. Cazamian,[3] however, adopting the sphenoidal route, successfully tapped the basal cisterns by inserting the needle from in front below the eye. The space between the occiput and atlas has been used for drainage of the spinal fluid by Cushing and also by Haynes, but these operators resorted to the open methods of the early experimentalists. In several cases of meningitis in which lumbar puncture failed to yield fluid, Herrick[8] found at autopsy the adhesions preventing the communication between the spinal and cranial subarachnoid spaces to be around the foramen magnum. In one of these he reports an unsuccessful attempt to reach the cistern through the occipito-atlantoid ligament.

The following case, observed on the medical service at Camp Jackson, S. C., is given here through the courtesy of Major W. W. Herrick, and illustrates, in spite of the subsequent fatal issue, the clinical use of the occipito-atlantoid puncture when blockage occurs in the spinal canal. This patient having, under venous and subarachnoid serum therapy, apparently recovered from an attack of epidemic meningitis, suffered a relapse one month later. At this time lumbar puncture failed to produce more than 5 c.c. of fluid, and as the man was rapidly becoming worse, an attempt was made to break up the adhesions around the foramen magnum by rotating the head on the spine while the patient was under an anesthetic. This failed to accomplish its purpose and repeated lumbar punctures during the following ten days netted but 5 to 10 c.c. at a time. Although the relief of pressure occasioned by the release of even these small quantities was followed by a transient improvement in his condition at first, he eventually developed a stupor from which it was impossible to arouse him. The patient's condition was so grave that an attempt at least to relieve his condition by occipito-atlantoid puncture was justifiable. Accordingly, he was given a light chloroform anesthesia and the operation performed. The procedure was successful; 40 c.c. of turbid but blood-free fluid were obtained and 25 c.c. of serum injected, following which the patient became conscious and showed marked improvement. About twenty-four hours later (before the procedure could be repeated) death occurred. At autopsy a lumbar puncture yielded a few drops of very yellow amber fluid. In order to demonstrate the suspected block of the spinal canal, 35 c.c. of ink were injected with a syringe into the subarachnoid space through the lumbar needle. Following this a needle was inserted into the cistern and about 10 c.c. of turbid, blood-free fluid showing no traces of ink were aspirated. On exposing the spinal cord the canal was normal and on opening the dura the space beneath was entirely free of exudate. Beneath the arachnoid the ink was found to have stopped abruptly at the level of the sixth thoracic vertebra. The arachnoid was milked from below upward to see if the ink could be forced farther up the cord, but this manipulation resulted merely in ballooning out of the arachnoid at the upper limit of the injection without further upward passage of the ink. Above the line of injection, where the pathology was not obscured by the ink, the subarachnoid space was completely filled with a very thick fibrinous exudate, which in itself would be a marked hindrance to the free passage of the fluid within the membrane. The brain was then removed and examination of the structures in the canal at the level of the occipito-atlantoid articulation showed no evidence of injury by the puncture done the day before and no trace of the ink injected postmortem into the lumbar subarachnoid space.

A recent personal communication from Major Herrick informs us that he has since performed the operation successfully on a patient having streptococcus meningitis.

Another use of the procedure, especially in those cases of septic purulent meningitis other than of meningococcus origin, will be found by combining it with lumbar puncture for instituting an irrigation of the spinal canal. The value of irrigating the canal and thus getting rid of a large part of the pus and debris contained in it during infection has been recognized as a logical surgical procedure by Cushing and Sladen,[5] Aubertin and Chabanier,[1] Capitan[2] and others. These investigators made use of a retrograde lavage, the method being to inject suitable amounts of a bland solution in the lumbar region until the canal was filled. The solution was then permitted to flow off again at the lumbar needle and the process was repeated until the returned fluid was clear. The method has a disadvantage in that during the first injection infected debris may be shoved ahead of the fluid and find lodgment higher up in the canal if not at the base of the brain. Later, Franca[7] and Miller[10] went a step farther and used two needles, one inserted in the lower thoracic and the other in the lumbar region, passing a stream of Ringer's solution between them. We have been able to irrigate living cats from the cistern to the lumbar region and in the opposite direction with ease and for long periods of time; also in the cadaver the procedure has been found quite simple. Early in the summer of 1918 there was referred to us, through the courtesy of Major Joseph C. Bloodgood, a patient in whom the application of the combined occipito-atlantoid and lumbar puncture for a complete irrigation of the spinal meninges might be applied. The case was that of a man who, secondary to a basal fracture, developed a streptococcus meningitis, which at the time he was seen by us had advanced so far that there was little chance of benefiting him much by any procedure. With the patient under light chloroform anesthesia the lumbar and cistern punctures were accomplished without difficulty and the purulent spinal fluid was allowed to flow from both needles until the subarachnoid cavity was fairly well depleted. The upper needle was connected with a reservoir containing warm Ringer's solution, which was introduced into the subarachnoid space under about 100 mm. water-pressure. The flow between the needles was very satisfactory and a great quantity of additional pus was removed by the irrigation, which lasted about five minutes. Unfortunately, the procedure could not be repeated on this patient, who died about twenty-four hours later, but the single experience was useful in demonstrating the feasibility of the operation, and the ease with which the occipito-atlantoid puncture was accomplished recommends its use in similar cases.

With increase in our experience in the use of this method it is

entirely possible that this route should prove of value for the introduction of serum early in epidemic meningitis for the following reasons: The ordinary dosage (25 to 40 c.c.) of serum given at the lumbar region is not sufficient to fill more than the subarachnoid space of the cord, a fact that has been demonstrated in this laboratory by injecting similar doses of detectable suspensions into the lumbar canal of cadavers. In the case of a well-developed adult man, recently dead, such an injection of 30 c.c. of India ink were found to have blackened the entire subarachnoid space of the cord, but to be thinned out over the base and not visible at all over the convolutions. Proportionate doses of the same material were given both by the occipito-atlantoid and the lumbar routes to living cats shortly before they were sacrificed. In these it was found that the spread from the lumbar needle had reached in marked concentration as high as the foramen magnum, but around the base of the brain the ink particles were present only in great dilution. On the other hand the ink injected at the occipito-atlantoid ligament completely filled all of the basilar cisterns and extended well over the convexity of the brain. In accordance with the frequent finding of the earliest lesions of meningitis over the cortex, and because of the fact that serum administered at the lumbar region frequently fails to clear up the infection in the brain, these experiments suggest that an injection of serum given directly into the cistern early in the disease would be of great benefit. Koplik,[9] discussing epidemic cerebrospinal meningitis, emphasizes the tendency in children toward early blockage of the cerebrospinal fluid spaces and hydrocephalus formation, and appeals for some method of administering serum in the meninges other than by lumbar or ventricular punctures.

In conclusion, it may be said that puncture through the occipito-atlantoid ligament offers a convenient method for obtaining cerebrospinal fluid from laboratory animals; it has also been found more satisfactory than lumbar puncture in obtaining fluid at the autopsy table. After study of the anatomical relations of the cisterna in man, and after numerous successful punctures on the cadaver, we believe that the operation in skilled hands is a safe one for clinical use. We do not wish to minimize the possible harm which can result from such puncture; on the other hand, we are convinced that the technic is not difficult and that practice upon the cadaver will be convincing on this point, without which preliminary study the operation should not be performed.

Clinically, the procedure should prove useful (1) in reaching the upper fluid reservoirs of the central nervous system after blockage of the spinal subarachnoid space; (2) in combination with lumbar puncture for irrigation of the spinal subarachnoid space; and (3) in affording a method whereby specific therapy could be given more efficiently in early meningitis.

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ACUTE HEMATOGENOUS STREPTOCOCCIC PERITONITIS.

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Definition. Acute hematogenous streptococcic peritonitis is the designation used by the writer in cases produced by a streptococcus infecting the peritoneum by way of the blood stream without an apparent intermediary lesion of an abdominal viscus being demonstrable.

Primary Peritonitis. Authorities are divided as to whether a true primary peritonitis exists. Medical literature is meager in reports. Lewi,[1] Meade,[2] Collie[3] and Semple[4] described several

[1] Tr. Med. Soc. New York, 1873, p. 143.
[2] British Med. Jour., 1876, ii, 393.
[3] Med. Exam., 1877, ii, 843.
[4] Ibid., 1878, iii, 553.

cases and attributed the peritonitis to exposure. Grawitz,[5] in 1886, reported 13 cases of "idiopathic" peritonitis. In 1893 Tavel and Lanz[6] divided the peritonitides into a primary group and other numerous secondary groups classified according to the viscus harboring the causal focus. Flexner,[7] in 1898, simplified the classification by subdividing all secondary cases into an exogenous and endogenous type, depending on whether the infection reached the peritoneum directly from without (*e. g.*, operation, stab wound, lesion of the abdominal wall) or from a lesion of an abdominal organ. The primary cases he attributed to infection carried to the peritoneum through blood or lymph channels.

In 1901 Nothnagel[8] denied the possibility of such an entity as primary peritonitis. In a case in which streptococci were present in the throat and peritoneal exudate, he claimed that the organism had been swallowed with the sputum and wandered out through the intact stomach wall thus reaching the peritoneum. Sheldon[9] believed these cases had their origin in microscopic lesions of the appendix or other abdominal organs. Armstrong[10] insisted on the Fallopian tubes being the seat of the primary infection, because his cases of primary peritonitis all occurred in females. Wilder[11] believed they were secondary to throat lesions. Bond[12] and Jensen[13] maintained that microscopic intestinal lesions could initiate many of these primary cases of peritonitis.

Jensen fed some animals with virulent cultures of pneumococci in capsules. One of the animals died. At the postmortem examination a purulent peritonitis was found. A follicular enteritis with slight necrosis of Peyer's patches was present, but there was no ulcer or perforation. Pneumococci were found in the intestinal canal, intestinal wall, blood and peritoneum. Flexner,[14] in 1895, mentions the finding of diplococci in the lumen of the intestine, mucosa, submucosa and within the peritoneum in certain cases of infection of the intestine. These organisms were also present in lymphatic spaces, which he believed were the avenue of transit into the peritoneal cavity. He,[15] however, stated that while it would be possible for organisms to wander out through the normal intestinal wall, no definite proof of such an occurrence had yet been offered. Flexner believed that in all cases wherein the intestine was responsible a gross pathological lesion was present. Abacoumova[16] reports a case

[5] Charité Ann., 1884, xi, 770.
[6] Mitt. a. klin. u. med. Instituten d. Schweiz, 1893, i, 1.
[7] Philadelphia Med. Jour., 1898, ii, 1019.
[8] Wien. med. Presse, 1901, xlii, 1321.
[9] Med. Rec., New York, 1902, lxii, 394.
[10] Montreal Med. Jour., 1903, xxxii, 728.
[11] Tr. Chicago Path. Soc., 1916, x, 46.
[12] British Med. Jour., 1905, ii, 232.
[13] Arch. f. klin. Chir., 1903, lxix, 1134; Ibid., lxx, 91.
[14] Bull. Johns Hopkins Hosp., 1895, vi, 64.
[15] Flexner: Loc. cit.
[16] Thèse. de Lausanne, 1905.

in which streptococci were present in the intestinal wall. Lennander's[17] case was one of follicular enteritis.

The theories of gastric or intestinal causation appear disproved by the reports of cases of primary peritonitis in which the causative organism has at an early stage been recovered from the blood. Künzel's[18] case, in which most thorough gross, microscopic and bacteriological studies were made at the postmortem examination, furnishes us with absolute evidence as to the direct infection of the peritoneum by way of the blood stream from the nasopharynx without an intermediary abdominal lesion. Appendix, spleen, intestine, uterus, tubes and ovaries were all normal. On culture these organs proved sterile, or, as in the case of the intestine, yielded no organisms of the streptococcic group. The streptococcus was recovered only in the nasopharynx and peritoneal exudate.

Type of Primary Peritonitis. The type of primary peritonitis mentioned by Flexner, Manahan[19] and Fishbein[20] occurred exclusively as a terminating infection in chronic disease—*e. g.*, valvular defects, chronic parenchymatous nephritis, arteriosclerosis, cirrhosis of the liver and visceral carcinomata. The writer has studied 8 cases of primary peritonitis, all due to the streptococcus, that were entirely of a different character. Seven occurred in females and only one in the male. Their ages ranged between ten months and twenty-one years. They were in the best of health when stricken with this disease. In no instance could the peritonitis be ascribed to a metastatic process in an abdominal organ the result of a septicemia or pyemia. Metastatic foci in abdominal organs are rare in cases of general streptococcic infection.[21] This is offered as an explanation for the absence of any other abdominal lesion in this series. This is quite the opposite with staphylococcic infection, the presence of pyemic visceral processes being the rule. Ehringer,[22] in 1906, collected 21 cases of a similar type to that mentioned by the writer. Holt,[23] Martin,[24] Monks,[25] Bonnet,[26] Oppenheimer[27] and Dowd[28] have each recorded cases since Ehringer's report.

We believe that an acute inflammation of the nasopharynx, particularly of the tonsils, served as the original focus from which virulent organisms passed into the blood stream, reached the peritoneum and through their activity set up a violent peritonitis. We know that the peritoneum is, as a rule, unusually resistant to infection. What lowers the resistance of the peritoneum in these cases?

[17] Upsala Läkaref. Forh., 1900, vi, 248.
[18] München. med. Wchnschr., 1904, li, 1920.
[19] Boston Med. and Surg. Jour., 1905, clii, 346.
[20] Am. Jour. Med. Sc., 1912, cxliv, 502.
[21] Monographic Medicine, 1916, ii, 185.
[22] Thèse de Paris, 1906.
[23] Arch. Pediat., 1906, xxiii, 268.
[24] Ann. Surg., 1906, xliv, 917.
[25] Ibid., 1908, xlvii, 964.
[26] Lyon Méd., 1906, cvii, 821.
[27] Deutsch. Ztschr. f. Chir., 1906, lxxxiii, 456.
[28] Ann. Surg., 1908, xlviii, 821.

Shall we in accordance with the view that has been expressed by Rosenow claim that this particular type of streptococcus has a selective affinity for the peritoneum? Animal experimentation by Chapelle[29] in 1907 failed to establish any such selective affinity.

Relationship to Epidemic Streptococcic Sore-throat. Some dozen or more epidemics of septic throats are on record.[30] In those of recent years bacteriological studies have invariably proved a streptococcus as the offending organism. Capps[31] described it as a hemolytic capsulated streptococcus. Davis and Rosenow[32] found it to be a peculiar streptococcus. Later, Davis[33] acknowledged its close relationship to the Streptococcus hemolyticus and thought that the two were probably identical. This fact is of extreme importance, for although our cases did not occur during an epidemic of streptococcic sore-throat, yet the throats and peritoneal fluids yielded an identical coccus. We know that the Streptococcus hemolyticus sets up sporadic cases of tonsillitis and peritonitis. May not this organism, just as in the epidemics, infect the human body through milk and its products or by way of human carriers, be they handlers of infected dairy products, or those who have been in contact with cases of streptococcic angina?

Thorough clinical studies have, as a rule, not been made in these epidemics. Excluding Chapelle's investigations there is but scant mention of streptococcic peritonitis. The latter made a close study of the epidemic of septic throat which occurred in Helsingfors, Finland, in 1904. He reported eighteen cases of acute diffuse peritonitis, fourteen of which were beyond question secondary to angina of streptococcic origin. The most careful bacteriological studies were made. These proved beyond doubt that he was dealing with a streptococcus and not a pneumococcus infection. Mann[34] in his report does not mention the causes of the four deaths in the Concord, N. H., outbreak. Hamburger[35] records 9 cases of fatal peritonitis in the Baltimore epidemic. Invariably when looked for in these cases the streptococcus was found in the peritoneal fluid or venous blood at autopsy examination.

Etiologic Data. Seven of the writer's eight cases occurred in females. Isolated cases occurring in males are recorded in the literature. Our cases were all in the young; their ages ranged from ten months to twenty-one years. All occurred during the winter and spring months. This corresponds exactly to the seasonal incidences of the streptococcic throat epidemics. Longcope and Fox[36] have

[29] Arb. a. d. Path. Inst. d. Univ. Helsingfors, 1907, Bd. ii, p. 583.
[30] Bull. Johns Hopkins Hosp., 1913, xxiv, 1.
[31] Jour. Am. Med. Assn., 1912, lviii, 1111. Capps: Jour. Am. Med. Assn., 1912, lxi, 723.
[32] Jour. Am. Med. Assn., 1912, lviii, 773.
[33] Ibid., 1912, lviii, 1852.
[34] Jour. Infect. Dis., 1913, xii, 481.
[35] Loc. cit.
[36] Bull. Ayer Clinical Lab., Pennsylvania Hosp., 1906, No. 3, i, 111.

found the Streptococcus hemolyticus occasionally in the throats of healthy individuals and have demonstrated that the virulent forms are more common in the mouths of healthy persons during the cold months. Throat cultures when done in our cases have yielded a streptococcus in pure culture.

ANGINA. In but few instances was there a history of pain in the throat or tonsillitis. By the time the patients were admitted to the hospital all evidence, except for an intensely hyperemic pharynx, were usually absent. In a few cases the gravity of the abdominal condition unfortunately caused one to pay but scant attention to the throat. Whether or not a previous exudate had been present is difficult to say. It is possible that in those cases there had been no reaction on the part of the tonsils and the streptococcus gained easy access to the blood stream. Marked enlargement of the cervical glands was absent in our series, evidence of nature's failure of defence against systemic invasion.

PERITONITIC STAGE. The history, as a rule, was that the patient had suddenly, while in the best of health, been taken sick with high fever, reaching 104° F., or over, severe generalized abdominal pain, repeated vomiting and marked prostration. These phenomena persisted until admission. When the peritonitis followed a distinct anginal attack we frequently found that a period of well-being, lasting three or four days, intervened before the sudden development of the peritonitic symptoms. The temperature remained high without marked oscillations. The pulse was invariably very rapid and out of proportion to the temperature. It was at first of a bounding character. Herpes labialis was invariably absent in our series. Chapelle records its occurrence in a few instances.

Diarrhea occurred in but few of our cases. This is in contrast to the cases reported in the literature. Diarrhea is frequently stated to have preceded the peritonitis. This fact might argue for an intestinal origin in these instances. The leukocyte count was very high, ranging between 25,000 and 64,000, on the average 40,000. The polynuclear count varied from 85 to 97 per cent., on the average 92 per cent.

The abdomen was tender and moderately rigid all over. There was no marked distention, and careful examination only infrequently revealed evidences of fluid in the flanks. The patient rapidly passed into the terminal phase of peritonitis, with the usual attendant phenomena of Hippocratic facies, livid, clammy extremities and running, thready pulse. Death occurred in from three to eight days of the onset of the peritonitic stage, and was the result of cardiac and vasomotor collapse, induced by a virulent toxemia.

Ehringer mentions three cases of subacute character which developed localized abscesses and recovered after incision and drainage. These were all of mild character, without prodromal signs, slight if any vomiting, and prompt subsidence of fever.

Blood Culture. Blood cultures were taken during life in but four of our cases. In only one was a positive culture obtained, which showed a streptococcus in pure culture. In this case a blood culture had been taken thirty-six hours after the onset of the illness. This corresponds to Libman's[37] findings of sterile cultures in his cases of acute terminating peritonitis occurring in chronic parenchymatous nephritis. Cultures would very likely yield positive results more often if they could be taken at the very inception of the peritonitic process and not on the second to fourth day after, as was unfortunately the case in our series. Chapelle in one instance recovered the streptococcus on the fifth day of the disease, which was one day after operation and two days before exitus. These instances of positive blood cultures during the course of the peritonitis are the only ones to be recorded in literature. A positive blood culture, especially very early in the course of the disease, speaks very forcibly for the hematogenous origin of the peritonitis, and cannot be ascribed to an agonal bacteremia.

Prognosis and Treatment. Because of the absence of any primary focus that can be surgically evacuated the prognosis must of necessity be bad. Ehringer's 3 cases of localized abscess formation recovered after operation and drainage. Five cases of Chapelle's group were operated upon and all died. In the Chicago epidemic, Capps and Miller[38] reported nine deaths from streptococcic peritonitis. They failed to mention if there were any cases that recovered. The inference is that all who developed this complication died. Early operation and drainage of the peritoneal cavity is indicated. This has resulted in the saving of 2 of our 8 cases, an unusually high percentage of recoveries. In these 2 cases the throat lesions and glands of the neck were markedly in evidence.

Operative Findings. The peritoneal exudate varied from that of a thin serofibrinous to a fibrinopurulent character. Though Flexner, Manahan and Fishbein have, in the secondary peritonitides, shown that the character of the fluid is, as a rule, independent of the type of organism the peritoneal exudates of our cases were only exceptionally of the thick creamy character noticed in our primary pneumococcic cases. The peritoneal fluid yielded the Streptococcus hemolyticus in pure culture in seven cases and associated with the Bacillus coli in one case. This is highly instructive as compared with the fairly frequent finding of multiple organisms in the cases of peritonitis secondary to a lesion of an abdominal viscus. Monoinfection of the peritoneum would therefore strongly argue for a hematogenous source of infection.[39] As the Bacillus coli is seldom present in the blood infections it is highly probable that it was present as a secondary invader in the peritoneal exudate of our case.

[37] Bull. Johns Hopkins Hosp., 1906, xvii, 215.
[38] Loc. cit.
[39] Wilder: Tr. Chicago Path. Soc., 1916, x, 46.

Thorough search was made at operation for any gross visceral abdominal lesion. In no instance at operation or postmortem have we been able to find anything that could be accused of being the lesion responsible for the peritonitis; nor were there any evidences of cirrhosis, cardiac defect, chronic nephritis or other chronic disease present. These cases were therefore distinct from the terminating primary peritonitis of Flexner and closely allied if not identical with the streptococcic peritonitis found during epidemics of sore-throat.

Differential Diagnosis. Terminating primary peritonitis is superimposed on some chronic disease and occurs in either sex, while streptococcic peritonitis of the type herein described occurs in the previously healthy and almost exclusively in young females.

Pneumococcic peritonitis is in one-third of the cases secondary to pneumococcic lesions in the lung or pleura. The onset is stormy and the course of the disease is milder. The temperature is lower. Herpes is frequent. Subacute cases with localized peritonitis are more common, and these have a creamy, thick, peritoneal exudate. The prognosis is better. Throat cultures and peritoneal fluid show a pneumococcus on careful bacteriological examination. The streptococcic cases have a less sudden and milder onset, a prodromal period of angina, malaise and abdominal cramps. The course is very severe, nervous symptoms of toxemia are more marked and diarrhea may occur early and be persistent.

Pneumonia with pneumococcic appendicitis yields, besides the evidences of pneumonia, distinct localized rigidity and tenderness in the right lower abdomen.

Acute appendicitis, with subsequent general peritonitis, at the onset shows normal or only slightly elevated temperature. There is but slight vomiting. Diarrhea is rare. There is no marked prostration early; the pulse is then not very rapid and the rigidity for a considerable time is localized in the right iliac fossa.

Acute perforative peritonitis gives a history of a primary focus in a hollow viscus, *e. g.*, gastric or duodenal ulcer, gall-bladder disease, or intestinal lesion. The onset is marked by a very severe pain localized at the site of perforation. The temperature at the beginning is normal or subnormal. The abdomen during the first few hours is not rigid all over. The pulse-rate is not rapid until late. A secondary stage of apparent improvement occurs before the final general peritonitis supervenes. There is no diarrhea.

Acute gonococcic peritonitis gives previous symptoms and signs referable to the uterus or adnexa. Vaginal smears may yield gonococci. There is no marked abdominal rigidity. The symptoms usually abate in twenty-four hours. The great majority of cases recover. The temperature and pulse are lower. The peritoneal exudate is mostly in the pelvis and is usually of a dry fibrinous character, only occasionally purulent.

Typhoid peritonitis usually occurs late in the course of the disease. The enlarged spleen, positive Widal, typical roseola and blood culture assist in the differential diagnosis.

Localized tuberculous peritonitis is with difficulty to be distinguished from localized forms of streptococcic peritonitis.

Streptococcic sepsis is secondary to a suppurative focus in the body, is frequently complicated by acute endocarditis and blood cultures are repeatedly positive.

CASE I.—Sadie F., J. H. No. 25993, aged five years, was admitted into the service of Dr. William Linder on May 12, 1914. Two days ago she began to suffer with severe abdominal cramps, constipation, high fever and vomiting. These persisted on admission. She appeared splendidly nourished. Her cheeks were flushed. The abdomen was tender and showed a doughy rigidity all over. Temperature, 104° F., pulse, 160; respirations, 23. An enema resulted in the passage of sour smelling mucus accompanied by a few particles of feces. The urine showed a heavy trace of albumin, many hyaline and granular casts and a moderate number of red blood cells. Leukocytes, 28,000; polynuclears, 94 per cent. Operation performed the same day revealed thin, creamy pus in the peritoneal cavity, omentum congested and all abdominal viscera negative. Examination of the pus from the peritoneal cavity revealed the Streptococcus hemolyticus and Bacillus coli. The patient died five days later. No postmortem examination was permitted.

CASE II.—Annie G., J. H. No. 29330, aged ten months, was admitted December 18, 1914, into the service of Dr. William Linder. She had been sick for a few days with a high fever and marked prostration. Examination pointed to a general peritonitis. Preoperative diagnosis was pneumococcic peritonitis. Leukocytes, 60,000; polynuclears, 85 per cent. Temperature, 103.6° F.; pulse, 176; respirations, 60. Operation was performed immediately. On opening the peritoneal cavity there was an escape of a large quantity of seropurulent fluid containing flocculi. The appendix and other viscera were found normal. The child did not react and died during the night. Culture of the peritoneal fluid yielded the Streptococcus hemolyticus.

CASE III.—Gertrude K., J. H. No. 37041, aged twenty-one years, was admitted into the service of Dr. Ronsheim on April 8, 1916. Appendectomy had been performed seven years ago. Menstruation was, as a rule, irregular and at long intervals. She had given birth to one child. Last menstrual period thirty-three days before admission. On the day before her entrance to the hospital she was suddenly seized with severe cramps, high fever and vomiting. The symptoms persisted on admission. She was restless. Cervical glands were palpable. The abdomen was slightly distended, very rigid and tender throughout. Temperature, 104° F., pulse, 152; respirations, 28. Leukocytes, 20,000; polynuclears, 93 per cent.

Urine showed a faint trace of albumin and a few pus cells. Blood culture was sterile. On the mistaken diagnosis of a peritonitis, secondary to a tubal condition, a vaginal section was performed three days after admission. A large amount of thin pus escaped. This on culture yielded the Streptococcus hemolyticus. She died three days later. Thorough postmortem examination revealed no primary focus in the abdominal cavity.

Case IV.—Lillian L., J. H. No. 31352, aged ten years, was admitted April 20, 1915, into the service of Dr. William Linder. One week before admission she was taken ill with a tonsillitis, which was treated for three days. After this period she felt well for two days. Two days before admission she was taken with a chill. Abdominal cramps, vomiting, constipation and high fever set in and persisted. Her face was flushed and cyanotic. The tonsils were large and together with the pharynx markedly congested. A few cervical glands were palpable. The abdomen was distended, slightly rigid and tender all over. Temperature, 105.8° F.; pulse, 160; respirations, 40. The urine was sterile on culture and yielded a trace of albumin. Leukocytes, 44,000; polynuclears, 96 per cent. A vaginal smear was negative for gonococci. Operation done on the same day failed to reveal any evident source for the marked general peritonitis present. A large amount of thin pus containing large green flocculi was evacuated. On culture this yielded the Streptococcus hemolyticus. The patient developed intra-abdominal collections of pus which caused a protracted temperature for one month. These collections were evacuated by means of the insertion of dressing forceps into the wound. The patient made a perfect recovery and was discharged cured just two months after admission.

Case V.—Minnie E., J. H. No. 41321, aged six years, was admitted January 27, 1917, into the service of Dr. William Linder. Abdominal pain, fever and vomiting set in thirty-six hours ago. The vomiting was repeated three times. Bowels moved with enema. On admission the abdomen was seen to be distended, with generalized rigidity and tenderness. Temperature, 104° F.; pulse, 160; respirations, 40 and labored. The child was pale, drowsy and restless. Blood culture revealed the Streptococcus hemolyticus. Urine showed evidences of a marked toxic nephritis, heavy trace of albumin, many hyaline and granular casts and marked acetone. Leukocytes, 64,000; polynuclears, 92 per cent. Vaginal examination showed no gonococci. Operation was performed three and one-half hours after admission. The appendix and all other viscera except for superficial congestion were normal. A moderate amount of serofibrinous flakes were present in the pus. The peritoneal fluid on culture revealed the Streptococcus hemolyticus. The child did not do well and died on the fourth day after operation.

Case VI.—Pauline E., J. H. No. 41424, aged nineteen years, was admitted into the service of Dr. William Linder, February 3,

1917. Three weeks ago she had suffered from general abdominal pains, which were intermittent in character. There were no gastric symptoms, no chills or fever. Her bowels were constipated. Three days ago she was suddenly seized with a dizzy spell, which was followed by persistent nausea and projectile vomiting. Paroxysmal generalized abdominal cramps were present. The temperature was high, ranging between 105° and 106° F. She had a persistent diarrhea, having five or six movements daily. There was no blood in the stool. On one occasion she vomited one-half tumblerful of clotted blood. This observation was made by her physician in attendance. These symptoms persisted to admission. Examination on admission to the hospital showed marked cyanosis and a state of collapse. The abdomen was tender all over. Shifting dulness was present. The extremities were cold and clammy. The patient was menstruating at the time. Blood culture taken the same day proved sterile. The urine showed a heavy trace of albumin and many hyaline and granular casts. Leukocytes, 40,000; polynuclears, 97 per cent. Temperature ranged between 102° and 104° F.; pulse, 120 to 160; respirations, 26. Herpes was absent. Lavage of stomach brought forth large amounts of foul light-brown fluid. The patient was moribund, and at the earnest request of the family that something be done, operation was performed the next day. On opening the peritoneum a large amount of non-odorous, seropurulent fluid escaped. The appendix, tubes, ovaries, stomach, intestines and kidneys were investigated and found normal. Some pus was removed for examination and yielded a pure culture of Streptococcus hemolyticus. The next day the patient died. Complete postmortem examination was made the next day. Absolutely no trace of anything that might be interpreted as being the primary focus was found in the abdomen. Special attention was paid to the generative organs, which were found normal.

CASE VII.—Bessie A., J. H. No. 41958, aged twelve years, was admitted into the service of Dr. William Linder, March 10, 1917. She had an attack of diphtheria at three years, and since then has a persistent discharge from both ears. She suffered from repeated attacks of tonsillitis. Six days before admission she suffered from sore-throat, fever and dysphagia. She felt better the next morning. The next three days she was somewhat feverish, but was up and about and attended school. On the day before admission she was seized with generalized abdominal pain, which were most severe about the umbilicus. She was feverish, vomited and her bowels moved several times after an enema. On the day of admission these symptoms together with a moderate diarrhea were still present. Examination revealed a well-nourished girl with flushed facies. The pharynx was reddened. No exudate on the tonsils was present. Mucopus hung down the posterior pharyngeal wall. The abdomen was not distended and was markedly tender over the lower half. Rebound

tenderness (Blumberg's sign of peritoneal irritation) was present. The temperature was 104° F.; pulse, 140; respirations, 32. The urine was negative. Leukocytes numbered 23,000; polynuclears, 89 per cent. Culture of the ear discharge yielded the Bacillus pyocyaneus and a Gram-positive coccus. Operation performed the same day revealed a normal appendix. The intestines were covered over with flakes of exudate. A large quantity of seropus was present in the pelvis. Thorough investigation revealed no primary focus. The peritoneal fluid on examination showed a Streptococcus hemolyticus. Throat cultures yielded the Streptococcus hemolyticus and Staphylococcus albus. A catheterized specimen of urine before operation showed Bacillus coli. Blood culture before operation proved sterile. The temperature and pulse stayed up for the first six days after operation and then reached normal. The patient made an uneventful recovery. Rectal examination on discharge failed to reveal any pelvic exudate such as might result from a residual abscess.

Case VIII.—Samuel E., J. H. No. 48864, was admitted April 7, 1918, into the service of Dr. J. B. Bogart. One week before admission the patient and his sister had partaken of some spoiled milk. They both vomited profusely. The girl was promptly relieved after rectal irrigations. The patient, however, developed a sore-throat and temperature of 103° F. The mother noticed that the child's abdomen became rigid. Generalized abdominal pain was complained of on the day of admission. Diarrhea was at no time present. On admission the child appeared very ill, with pinched facies, congested throat and marked generalized abdominal rigidity and tenderness. The urine was negative. The leukocytes numbered 28,800; polynuclears, 88 per cent. Temperature, 102° F.; pulse, 120; respirations, 30. Operation was performed the same day by Dr. G. I. Miller. The peritoneal cavity was filled with much seropurulent fluid. The appendix was kinked but not inflamed and was incidentally removed. Exploration revealed no primary focus. Two cigarette drains were inserted and the abdomen closed in the usual manner. The pus from the peritoneal cavity was carefully examined bacteriologically. An organism identical in its characteristics with the Streptococcus hemolyticus was recovered in pure culture. This organism showed no capsule, did not ferment inulin and did not dissolve bile. The temperature, pulse and respiration persisted high. Seven days after operation signs of pneumonia of the right upper lobe appeared. The child died four days later.

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PATHOLOGY OF (MUSTARD?) GAS INHALATION.

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Introduction. The object of this paper is to offer a description of the gross and microscopic pathology produced by the inhalation of (mustard[1]) gas. Of the 37 cases included in this study, 35, according to the field medical cards, were due to mustard gas, 1 to mustard gas and phosgene and 1 to phosgene alone. In 34 cases the action of the gas on the respiratory tract was the main factor in causing death. Two died as a result of extensive skin burns, and 1 of cellulitis of the face and neck following burns in this region. It is evident that though the skin and eyes suffer from contact with this agent, and though death may result from injury in these areas, inhalation and the resulting pathology in the respiratory tract is the important factor in cases which reached this center.

The respiratory tract is attacked from the tip of the epiglottis to the terminal bronchioles and air vesicles. The effects seen here are due (1) to the intense irritation and escharotic action of the gas, and (2) to secondary infection, which promptly occurs. As seen in the autopsy room, more or less of the entire mucosa over this region is covered by a fibrinopurulent exudate, a false membrane, from dirty gray to yellowish or greenish-yellow in color depending somewhat on the amount of suppuration and blood pigments present. In many cases it covers the entire area from the tip of the epiglottis downward; in others it is in patches; and in relatively few does it cover the wall of the lower part of the pharynx.

The appearance of this membrane, both grossly and microscopically is very similar to that usually seen in diphtheria. In addition, the clinical features are not unlike those in the laryngeal type of this disease: hoarseness, temperature and frequently a relatively rapid pulse. Also, throat cultures often showed that many of them harbored the typical organisms. As a result, it not infrequently happened that perplexity arose in the differential diagnosis and several times an erroneous diagnosis of diphtheria, or *vice versa*, was made.

In nearly all cases the larynx is attacked. Here the false membrane extends down into all the irregularities of this region. The reaction is usually accompanied by more or less edema surrounding

[1] The term "mustard" gas is used because of the statements found on the clinical records, together with the character of the lesions which corresponds to that described in the literature.

the base of the epiglottis, the aryepiglottic folds and the false vocal cords. When the membrane is removed a deeply injected, hemorrhagic surface is revealed, usually showing shallow ulcerations. These are particularly likely to occur along the prominent and more rigid portions, such as the tip of the epiglottis and the edges of the vocal cords.

In the trachea and larger bronchi, much the same pathology exists. There is the same sort of membrane with the injection, hemorrhage and ulceration of the underlying tissues. Here also the ulceration tends to occur on the more prominent portions, such as the mucosa over the cartilaginous rings.

In cases of longer standing the membranous exudate is less in evidence and the ulceration of the tracheal and bronchial walls is more marked. In one case (Fig. 1) the mucosa of the lower half of the trachea and of the bronchi in the region of the bifurcation was of a greenish hue and literally riddled with ulcers, one of which was 1 cm. in diameter and extended through the cartilaginous ring to the outer fibrous coat of the trachea.

The lungs are usually very voluminous, due to a marked emphysema, largely vesicular, but occasionally interstitial or bullous. Subpleural hemorrhages are frequent. There may or may not be a pleurisy depending upon the extent of the secondary infection present. There is commonly the nodular feel of a bronchopneumonia and occasionally the solidity of a massive consolidation. The cut surface is characteristic. In very mild or very early cases there may be only congestion, hemorrhages and edema of the parenchyma surrounding the bronchial tree, together with emphysema of the peripheral portions; but ordinarily the exudate described as occurring in the trachea and bronchi extends down to the finest radicles, which are not simply lined with the membrane but actually plugged. These plugs project above the cut surfaces and may be squeezed out, much like comedones. About many of these bronchioles there is a larger or smaller area of infiltration, resembling bronchopneumonia, raised, grayish or dark red (if hemorrhagic) and dry and granular in appearance. The hemorrhagic areas are prominent. Outside the pneumonic area is the vesicular emphysema.

In the older and more advanced cases necrosis is frequently present in the consolidated areas, and this becomes the more prominent feature. This occurs particularly nearer the hilus where the pneumonic areas are larger, confluent and massive, but may also be seen in the centers of the smaller discrete areas. The necrosis gives rise to abscess cavities, the larger of which have ragged, irregular walls and are filled with thin, grayish, granular, purulent and necrotic material.

Microscopically the pathology is very interesting. In the upper respiratory tract the membranous exudate lining the lumen is exactly similar to that seen in diphtheria, consisting of masses of fibrin

mixed with occasional leukocytes, cellular debris and plasma. On the free surface of this exudate numerous clumps of bacteria are seen, principally diplococci. There is often no differentiation between the exudate and the mucosa of the trachea or bronchi. The epithelium is nearly everywhere absent. In a few places degenerating or necrotic cells can still be made out. The submucous tissue is infiltrated with leukocytes and is definitely edematous. There is not quite as extensive hyalinization of the fibrin, however, as one finds in a diphtherial membrane.

This type of exudate extends down into the bronchioles, where at times the lumina are completely plugged. The exudate is frequently seen attached at only one point, and here the membrane blends with the wall of the bronchiole so intimately that no differentiation is possible. The wall is markedly infiltrated with leukocytes, and this condition extends into the contiguous alveoli. In the unattached portions of the bronchial wall the epithelium may still persist. It is at the point of attachment of the fibrinopurulent membrane that the ulceration and necrosis apparently begins, and from there it extends into the deeper portions of the lung parenchyma, resulting in the formation of abscesses of the lung. In the upper portion of the tract, namely, the prominent edges of the epiglottis, vocal cords and cartilaginous rings, similar ulcerations are encountered. These ulcerations may perhaps be explained by the fact that the portions protruding into the lumen are attacked by larger quantities or by more concentrated mixtures of the poisonous gases. It is not impossible that minute droplets of the liquid gas itself are inhaled. In the lower portion of the tract the direction of the air current may determine the site of greatest injury.

The histological picture varies, depending upon the rapidity of death after the injury and consequently on the dose and concentration of the inspired gas. In several cases that came to autopsy the dose was evidently overwhelming, resulting in death from the escharotic and irritating action alone. In these rapid cases the prominent features are the edema, the profound injection of the bloodvessels and the hemorrhage. The edema generally differs from ordinary pulmonary edema in that the fluid escaping into the alveoli is considerably more albuminous, so that when coagulated it greatly resembles colloid. The fluid not only fills the vesicles around the bronchioles, but often is seen separating the cellular structure of the alveolar walls. In areas farther away from the bronchioles the albuminous fluid is deposited principally in the neighborhood of the alveolar walls, leaving clear spaces in the centers of the vesicles. Some areas show marked fibrin deposits lining the walls of the alveoli in a manner similar to the exudate seen in the bronchioles or even in the bronchi. The only difference noticeable is that there is a relative absence of leukocytic infiltration. In the centers of these alveoli there may be only a thin serum deposited

or a very fine fibrinous network; sometimes the space is entirely free from exudate. In older stages the fibrin becomes hyalinized and shows an infiltration of leukocytes and the presence of degenerating desquamated epithelial cells.

Such a picture as above described helps explain the very marked dyspnea and cyanosis so frequently encountered in these cases clinically. Both the albuminous fluid around the walls of the air vesicles and the lining by dense fibrinous masses must produce a very profound interference with the normal interchange of gases in the alveoli.

Another marked feature is the injection of the bloodvessels. In many of the bronchial walls the enormously dilated capillaries present a picture of a capillary hemangioma. Also the extensive hemorrhage, which is so commonly seen in the alveoli surrounding the bronchioles, gives a picture, with the low power of the microscope, which resembles a cavernous hemangioma of the liver. The capillaries of the alveolar walls are dilated and tortuous. It requires very little imagination to visualize the processes by which the extensive hemorrhages occur.

The histology of the peripheral portions of the lungs shows little except vesicular emphysema. In later stages, with advanced pneumonic involvement, pleurisy may be present.

In the older cases, that is, in cases which die of the secondary infection rather than from the direct effects of the gas, there is a picture of bronchopneumonia. But even here the marked edema and hemorrhage, along with the peculiar deposits of fibrin, make the diagnoses fairly easy. Areas of necrosis are now present. These apparently begin in the walls of the bronchioles and extend centripetally, forming occasionally large abscesses filled with pus and necrotic debris. Around these necrotic areas the alveolar walls often show thickening due to fibrosis and infiltration, with round cells and polymorphonuclears. The alveoli contain dense masses of precipitated serum or fibrin in various stages of organization. Some show only a slight infiltration with leukocytes; others show fibroblasts from the alveolar walls invading the masses; still others show fairly well-advanced organization of the exudate. These areas are generally small and surround the bronchioles in the regions where the abscesses are apparent. The picture is unlike the ordinary types of organization pneumonias, in that the areas of necrosis and the abscesses are more common. Some of the bronchioles also show organization of the exudate, so that if the case should go on to healing the bronchioles would probably become organized into fibrous cords.

No changes were evident in the bronchial walls that could be taken for bronchiectases. However, the various lesions seen in the bronchi and bronchioles might lead to great weakening and dilatation if the patient should go on to recovery.

Case No.	Hosp. No.	Days after gassing	Skin and eyes.	Larynx.	Trachea.	Bronchi.	Bronchioles.	Lung.	Clinical data.	Cause of death.
1	25-27	18	Extensive burns; severe conjunctivitis	False membrane; hemorrhage; ulceration	False membrane; hemorrhage; ulceration	False membrane; hemorrhage; ulceration	Plugged with thick exudate	Small patches of consolidation	.....	Skin, burns of, extensive.
2	25-32	6	Severe second degree burn of face, neck, buttocks, thighs; severe conjunctivitis	Heavy false membrane; surface ulcerated; edema of glottis	Heavy false membrane; lower part hemorrhagic	Thin fibrinopurulent membrane	Many occluded by plugs of fibrinopurulent membrane	Edema; small patches of consolidation	Cyanosis; severe cough; pain in chest; albuminuria	Acute fibrinopurulent tracheobronchitis.
3	25-38	6	Skin mild, not extensive burns; eyes inflamed	Purulent exudate; hemorrhagic	Injected; thin fibrinopurulent exudate	Thick fibrinopurulent exudate	Many completely plugged with thick exudate	Marked edema; moderate patches of consolidation	Fever; eyes swollen; pain in chest; delirium	Acute hemorrhagic and purulent tracheobronchitis.
4	25-39	6	Mild skin burns	Thick purulent exudate; hemorrhage; ulceration	Thick purulent exudate; hemorrhage; ulceration	Thick purulent exudate; hemorrhage; ulceration	Many completely plugged with thick exudate	Emphysematous; small nodules of consolidation	Fever; dyspnea	Acute ulcerative and suppurative tracheobronchitis.
5	25-40	20	.....	Congested; thin layer of purulent exudate	.....	Congestion; fibrinopurulent exudate	Congested fibrinopurulent plugs	Small patches of bronchopneumonia; edema	Temperature; swelling of eyes; bronchitis and pulmonary edema	Acute suppurative laryngitis and bronchitis; bronchopneumonia.
6	25-45	29	Large superficial skin burns; eyes congested and lids ulcerated	Injected; thickened; yellow thick purulent exudate; ulceration	Injected mucosa thickened	Fibrinopurulent membrane	.....	Diffuse bilateral bronchopneumonia; edema; emphysema	Cyanosis; dyspnea; conjunctivitis; signs of bronchopneumonia	Acute suppurative tracheobronchitis and ulcerative laryngitis; bronchopneumonia.
7	25-48	17	Severe burns of genitals; eyes acutely inflamed	Ulceration; hemorrhage	Thick fibrinopurulent membrane; hemorrhage; ulceration	Thick fibrinopurulent membrane; hemorrhage; ulceration	.....	Diffuse bronchopneumonia; emphysema marked	Fever; cyanosis and dyspnea	Acute suppurative and ulcerative tracheobronchitis; bronchopneumonia.
8	25-50	12	Severe burns of face; severe conjunctivitis	Congestion; hemorrhage; thin yellow fibrinopurulent exudate	.....	.....	.....	Bronchopneumonia, diffuse; pulmonary necrosis; edema marked	Profuse expectoration; diffuse bronchitis; membrane on the soft palate	Bronchopneumonia and acute purulent tracheobronchitis.
9	25-56	10	Severe conjunctivitis	.....	Thin yellow exudate; hemorrhage; ulceration	Thin yellow exudate; hemorrhage; ulceration	.....	Bronchopneumonia, diffuse emphysema and edema marked	Fever; cyanosis; dyspnea; diffuse bronchitis	Acute suppurative tracheobronchitis and bronchopneumonia.
10	26-16	3	Mild skin burns; severe hemorrhagic conjunctivitis	Hemorrhage; ulceration; purulent exudate; edema of glottis	Hemorrhage; ulceration; purulent exudate	Hemorrhage; fibrinopurulent exudate	Many completely plugged with thick exudate	Early bronchopneumonia; marked emphysema	Coma; dyspnea; cyanosis; temperature and rapid pulse	Acute hemorrhagic and suppurative tracheobronchitis and edema of glottis; bronchopneumonia.

11	26–18	4	Burn of genitalia; severe conjunctivitis	Hemorrhage; edema; plastic exudate	Hemorrhage; edema; plastic exudate	Hemorrhage; edema; plastic exudate	Many completely plugged with exudate	Early bronchopneumonia; marked emphysema	Cyanosis; dyspnea	Acute hemorrhagic and suppurative tracheobronchitis; bronchopneumonia.
12	26–26	13	.....	.....	.....	Left has plastic exudate	.....	.....	Temperature; dyspnea; albumin and casts	Acute fibrinous bronchitis and edema of lungs.
13	26–30	17	Severe second degree burns; severe conjunctivitis	.....	.....	Congested; moderate purulent exudate	Congested	.....	Burns of skin only	Severe skin burns.
14	26–44	5	Severe conjunctivitis	Fibrinopurulent exudate	Congestion and fibrinopurulent exudate	Congestion and fibrinopurulent exudate	Purulent exudate	Massive bronchopneumonia	Cyanosis; dyspnea	Bronchopneumonia; suppurative bronchitis and tracheitis.
15	26–46	6	Congestion and hemorrhage in the conjunctivæ	Fibrinopurulent exudate	Fibrinopurulent exudate	Fibrinopurulent exudate	Many plugged with heavy fibrinopurulent exudate	Moderate bronchopneumonia; edema	Dyspnea; conjunctivitis	Acute fibrinopurulent tracheobronchitis; bronchopneumonia.
16	26–52	10	Second degree burns of scrotum; severe conjunctivitis	Hemorrhage; ulceration; fibrinopurulent exudate	Hemorrhage; ulceration; fibrinopurulent exudate	Hemorrhage; ulceration; fibrinopurulent exudate	Purulent exudate	Bronchopneumonia	Fever; sore throat; signs of pneumonia	Acute suppurative ulcerated tracheobronchitis; bronchopneumonia.
17	26–56	9	Slight skin burns; marked acute conjunctivitis	Thick exudate; vocal cords edematous and ulcerated	Heavy fibrinopurulent exudate	Casts of bronchi in pseudomembrane	Plugged with thick exudate	Early bronchopneumonia	Dyspnea; cyanosis; fever; signs of pneumonia	Diphtheria; edema of glottis; acute suppurative and ulcerative tracheobronchitis; bronchopneumonia.
18	26–59	25	Moderate skin burns; ulceration of eyelids	Plastic exudate; ulceration	Marked fibrinopurulent exudate	Very marked fibrinopurulent exudate	Many completely plugged with thick exudate	Marked bronchopneumonia	Fever; dyspnea; cough	Acute ulcerative and membranous tracheobronchitis; bronchopneumonia.
19	26–62 A.	21	Moderate skin burns; ulceration of lids	Fibrinopurulent pseudomembrane	Hemorrhage; ulceration; fibrinopurulent exudate	.....	Pus	Advanced bronchopneumonia; necrosis (early)	.....	Bronchopneumonia; ulcerative and membranous tracheobronchitis.
20	26–74	17	.....	Fibrinopurulent pseudomembrane	Fibrinopurulent pseudomembrane	Pseudomembrane and pus	Many plugged with thick exudate	Early bronchopneumonia; edema; emphysema	Fever; hoarseness; cough; pain in chest; dyspnea	Acute suppurative tracheobronchitis; bronchopneumonia.
21	26–1	11	Severe skin burns of face and neck; eyes burned	.....	.....	.....	.....	.....	.....	Cellulitis of face and head following burns in these regions.
22	49–32	7	Severe skin burns; eyes injected	Thick fibrinopurulent exudate; ulceration; hemorrhage	Thick plastic exudate; ulceration; hemorrhage	Thick plastic exudate; ulceration; hemorrhage	Many plugged with thick exudate	Edema	Dyspnea; pain in chest; weak pulse	Acute fibrinopurulent tracheobronchitis.
23	49–34	4	Severe, not extensive burns; purulent conjunctivitis	Thick fibrinopurulent exudate; ulceration	Thick fibrinopurulent exudate; ulceration	Thick fibrinopurulent exudate; ulceration	Pus	Hemorrhage	Cough; dyspnea; cyanosis	Acute suppurative and ulcerative tracheobronchitis.

Case No.	Hosp. No.	Days after gassing.	Skin and eyes.	Larynx.	Trachea.	Bronchi.	Bronchioles.	Lung.	Clinical data.	Cause of death.
24	49–36	5	Slight burns of face; eyes swollen	Greenish-yellow fibrinopurulent exudate	Greenish-yellow fibrinopurulent exudate	Greenish-yellow fibrinopurulent exudate	Plugged with similar exudate	Bronchopneumonia moderate; edema	Fever; delirium; eyes swollen	Acute suppurative and ulcerative tracheobronchitis; bronchopneumonia.
25	49–51	7	.....	.....	Fibrinopurulent pseudomembrane	.....	Plugged with similar exudate	Bronchopneumonia; marked edema; emphysema	Fever	Acute fibrinopurulent tracheobronchitis and bronchopneumonia.
26	49–67	25	Mild burns of head, chest, arms; conjunctivitis	Fibrinopurulent exudate	Fibrinopurulent exudate	.....	Many plugged with similar exudate	Bronchopneumonia; marked emphysema	.....	Acute fibrinopurulent tracheobronchitis and bronchopneumonia.
27	56–2	6	.....	.....	Congested	Hemorrhagic	Hemorrhagic	Marked edema	.....	Acute hemorrhagic bronchitis; edema of lungs.
28	56–7	?	.....	Fibrinopurulent membrane; congestion; edema	Fibrinopurulent membrane; congestion; edema	Congestion; edema	Congestion; edema	Very marked edema	.....	Edema of glottis.
29	56–14	16	.....	.....	.....	.....	.....	Bronchopneumonia	.....	Bronchopneumonia.
30	56–19	4	Skin of face slightly burned; corneal opacity	Fibrinopurulent exudate; ulceration; hemorrhage	Fibrinopurulent exudate; ulceration; hemorrhage	.....	Many plugged with similar membrane	Emphysema	.....	Acute suppurative and ulcerative tracheobronchitis.
31	56–30	18	Few mild burns; conjunctivitis	Thin fibrinopurulent exudate and ulceration; edema of glottis	.....	.....	Many plugged with similar exudate	Early bronchopneumonia	Fever	Suppurative tracheobronchitis;bronchopneumonia.
32	56–44	35	Conjunctivitis	Pseudomembrane (gas and diphtheria); edema of glottis	Fibrinopurulent membrane	.....	.....	Hemorrhage	Fever; diphtheria	Septicemia; diphtheria; acute fibrinopurulent tracheobronchitis.
33	56–57	34	Conjunctivitis	Fibrinopurulent pseudomembrane	.....	.....	Pus	Massive bronchopneumonia	Violent cough, burning in chest; aphonia; nausea and vomiting	Acute fibrinopurulent tracheobronchitis; bronchopneumonia.
34	56–	70	Acute conjunctivitis	.....	Numerous deep ulcerations	.....	Fibrinopurulent plugs and necrosis	Massive bronchopneumonia; abscess formation due to necrosis	.....	Gangrenous and ulcerative tracheobronchitis; lung abscess; bronchopneumonia.
35	19–1	?	Slight burns of face; congested conjunctivæ	.....	.....	Injected	Pus	Bronchopneumonia; emphysema marked	.....	Bronchopneumonia.

In one of the cases studied the condition had gone on for several months and yet no bronchiectases were apparent in the lungs. In the cases of influenza-pneumonias studied in this center, bronchiectatic changes were relatively common and were apparent in lesions of much shorter duration. It is therefore quite likely that the lung pathology following influenza is more susceptible to the development of bronchiectasis than that following gas inhalation.

The pathogenesis of these lesions cannot be completely worked out from the material obtained at this center, because no cases came to autopsy under four or five days after exposure. However, by correlating the findings, and by making a composite picture of all the lesions encountered in the various stages of the disease, one might visualize the processes of reaction about as follows:

As the irritating gas is inspired, some of the exposed cells may become immediately necrosed. The capillaries nearest the surfaces become engorged. This is true also in the smallest bronchioles and perhaps in the alveoli themselves. The irritation causes an exudate consisting of a moderate quantity of heavy albuminous fluid in contradistinction to the huge quantities of thin fluid poured out in cases of phosgene inhalation. Later, cellular elements appear in the exudate along with desquamated epithelial cells. Some of the fibrinogen is converted into fibrin, which forms a lining not only along the upper tube of the respiratory tract but also may extend down into the terminal bronchioles and air cells. Depending upon the amount of irritation, the exudate, which is now fibrinopurulent in character, may increase in thickness until it may produce a layer 3 or 4 mm. in depth in the larynx, trachea and bronchi. There is at the same time a marked edema and congestion of the loose subepithelial cellular tissues. In proportion to the amount of congestion and the extent of the necrosis produced will be the extent of the ulceration along the larynx, trachea and bronchi and the hemorrhages in the lung parenchyma. The amount of exudate in the smaller bronchioles may become so abundant as to completely plug the lumina. This obstruction of some of the bronchioles will result in the compensatory emphysema of other portions of the lung.

The upper respiratory tract is constantly exposed to infection, which will soon result in a superimposed inflammatory reaction, due to the bacterial invasion. This infective process will gradually descend into the bronchioles, owing to the lowering in the resistance of the tissues. It is at this time that polymorphonuclear infiltration may become very abundant and produce miliary or submiliary nodules, which finally may become confluent. Because the gas is in the greatest concentration in the upper portion of the respiratory tract the greatest pathological changes will be produced around the hilus. If the necrosis is very extensive, very profound ulcerations may develop in the trachea and larynx, which may almost penetrate the walls. In the lung parenchyma the necrosis will gradually

develop into areas of hemorrhage and into abscess formation after the necrotic area becomes secondarily infected with bacteria.

If the patient receives severe burns in the respiratory tract but is still able to live for any length of time, for example, several months, then the resulting lesions will present the large areas of consolidation, pneumonic in character, through which will be scattered large or small areas of necrosis, with abscess formation. The attempt at healing will manifest itself by the definite evidences of organization of the exudate and the fibrosis, as previously described.

The following brief protocols are presented to illustrate the conditions found at autopsy in several cases of gas inhalation in which death occurred from five days to over two months after the injury. The first case is of a very early type while the last is an old and very advanced stage of the disease. Only the important data are given; the negative findings are omitted.

CASE REPORTS.

CASE I.—Autopsy 26–16. E. B. P., Sergeant, Co. H, 306 Infantry, No. 1702538. Aged twenty-two years, white. Died September 28, 1918, at 6 A.M., at Base Hospital 26. Autopsied September 28, 1918, at 10 A.M. Capt. Moses Barron, M.C., pathologist.

"*Clinical Data.* This case is that of a young man admitted to Base Hospital 26 at 6 P. M., September 27, 1918, from Hospital Train No. 63, with a diagnosis of gas, deleterious, absorption of, inhalation and surface contact. Temperature was 98°, pulse 156, respiration 20. The field medical card had been lost in transfer to the train. History obtained stated that he had been gassed three days previously. He was comatose, markedly cyanotic and breathed with great difficulty. The throat was reddened and swollen. The eyes were closed with purulent exudate. There were rales throughout the chest, with bronchial breathing suggesting consolidation. Diagnosis (addition) was made of bronchopneumonia, left lower lobe. September 28, temperature was 99°, pulse 108, respiration 16. Death occurred at 6 A.M.

"*External Appearances.* There is purulent exudate on the conjunctivæ of both eyes, with accumulation at the margins of the upper and lower lids. Small hemorrhages are present on the ocular conjunctivæ laterally to the corneæ. There is a vesicle around the external meatus of the urethra, 2 x 3 cm., and one on the anterior surface of the tibia, 1 cm. in diameter, 7 cm. below the patella. There is another vesicle, 2 cm. in diameter, 1 cm. below the internal malleolus, left.

"*Organs of the Mouth and Neck.* On opening the trachea and larynx there is found marked edema of the mucosa and submucosa. Pin-point hemorrhages, with minute ulcerations, are scattered over the entire epithelium. A purulent exudate covers the surface, very

marked over the vocal cords and at the base of the epiglottis. This is firmly adherent to the epithelium. The vocal cords are greatly thickened and the glottis appears almost completely closed through the approximation of the swollen tissues covered by the exudate.

"Lungs: On opening the bronchi they are found to be almost completely filled with tenacious masses of exudate. In the smaller bronchioles these assume a pseudomembranous character. They extend into the still smaller bronchioles as solid plugs, completely closing the lumina. On stripping the exudate the epithelium throughout shows pin-point hemorrhages, with minute ulcerations.

"Left: The lower lobe is large and voluminous. The lower half is feathery. It contains several irregular collapsed areas, reddish brown in color, in contrast to the grayish pink of the rest of the lung. There are firm, irregular masses present, which on section are reddish brown in color and contain grayish areas, 1 to 5 mm. in diameter, from the centers of which pus escapes from the bronchioles. The lower margin of the upper lobe is firm but crepitates slightly. On section, quantities of faintly turbid, blood-tinged fluid escape.

"Right: The right lung has only two lobes. The lower lobe is voluminous, light and feathery. The lower surface of the upper lobe shows numerous air vesicles varying from pin-point size to 2 mm. in diameter, situated along the interlobular septa. On section, quantities of pus escape from the large bronchioles.

"*Anatomical Diagnosis.* Edema of glottis; acute suppurative and ulcerative tracheobronchitis; beginning bronchopneumonia; edema of lungs; acute vesicular and interstitial emphysema; edema and congestion of the brain; congestion of the kidneys; gas burns of the conjunctivæ and skin.

"*Probable Cause of Death.* Acute suppurative tracheobronchitis, with beginning bronchopneumonia and edema of the glottis, following gas inhalation."

Microscopic Study (Section 46). The bronchioles are lined with a fibrinopurulent exudate. Some bronchioles are completely plugged. The plugs present a denser infiltration with leukocytes. The mucosa is nearly everywhere absent and the walls are infiltrated with polymorphonuclears. The capillaries are intensely injected. The alveolar walls immediately surrounding the bronchioles also show this injection of the capillaries, but the air vesicles contain relatively very little exudate. A few of the bronchioles are surrounded by a narrow zone of alveoli filled with polymorphonuclear leukocytes and some fibrin. There are small patches of edema in which the albuminous precipitate is very dense, resembling colloid.

Another section of the same lung shows an almost similar picture, but the purulent exudate in the alveoli is somewhat more marked.

CASE II.—Autopsy 25-32. W. B., Corporal, Co. F, 26 Infantry, No. 284685. Aged twenty-three years, white. Died October 14, 1918, at 2.45 A.M. Autopsied October 14, 1918, at 11 A.M. Capt. Moses Barron, M.C., pathologist.

"*Clinical Data.* This is the case of a man who was admitted to Base Hospital No. 25 on October 10, 1918, with extensive skin burns (second degree) over the face, neck, buttocks and thighs, due to mustard-gas contact. Inhalation of the same gas caused a severe inflammatory condition of the respiratory passages. Upon admission the patient was cyanotic, coughed frequently and complained of pains in the chest. Urinalysis showed albumin in the urine and hyalin and granular casts. The patient died at 2.45 A.M. on October 14, 1918.

"Lungs: The lungs and organs of the neck are removed *en masse.* The pyriform sinuses are covered by a thick, fibrinopurulent membrane, which is firm and adherent. The epiglottis is thickened and covered by a similar membrane. The entire larynx, including the vocal cords, presents a thick, shaggy membranous exudate, which, when removed, leaves a congested, necrotic and somewhat ulcerated surface. Portions of the exudate extend for a short distance into the trachea. Farther down into the trachea the mucosa is hemorrhagic, purplish red in color and covered by a thin hemorrhagic and purulent exudate, which becomes more marked in the bronchi and bronchioles where it almost occludes the lumina. On section of the lungs the cut surfaces are mottled, dark brown and red, with yellowish plugs completely filling some of the small bronchioles. On pressure large quantities of frothy fluid flow from the cut surfaces. The organs crepitate only slightly. Some of the bronchioles are surrounded by small grayish yellow, firm areas. The pleura is covered by a thin layer of fibrinopurulent exudate.

"*Anatomical Diagnosis.* Acute fibrinopurulent, hemorrhagic and ulcerative tracheobronchitis, with moderate edema of the glottis; early bronchopneumonia, with edema and congestion of the lungs; acute fibrinopurulent pleuritis; diffuse colloid thyroid; superficial burns of the skin from poisonous gas; mild acute diffuse nephritis.

"*Probable Cause of Death.* Acute fibrinopurulent and hemorrhagic tracheobronchitis, with edema of the lungs and partial edema of the glottis following inhalation of poisonous gas."

Microscopic Study (Section 426). The bloodvessels throughout the section are dilated and engorged. The bronchioles are plugged with fibrinopurulent exudate. In two bronchioles these plugs are seen to be attached to the wall at one side, at which point the mucosa is destroyed and the wall is edematous and extensively infiltrated with leukocytes. Remnants of mucous membrane are to be seen on the remainder of the bronchial wall. The capillaries in the wall are markedly engorged with blood. About the bronchioles there is extensive hemorrhage into the alveoli. Patches of hemorrhage alternating with emphysematous areas are scattered throughout the parenchyma. In some portions of the section the alveoli around the bronchioles are filled with a purulent exudate.

CASE III.—Autopsy 26–62. A. R. B., Private, Co. I, 61 Infantry, No. 2253041. Aged twenty-two years, white. Died October 31, 1918, at Base Hospital 26. Autopsied November 1, 1918. Lieut. Oliver C. Melson, M.C., pathologist.

"*Clinical Data.* This case is that of a man who was admitted to Base Hospital 26, October 12, 1918, with a gunshot wound of the right lumbar region. He was suffering from absorption of gas, deleterious, mustard, by inhalation and contact. (Clinical record is not available.) Death occurred October 31, 1918.

"*External Appearances.* . . . There are superficial ulcerations of the ears, eyes, nose and mouth. The skin of the right hand and forearm, both legs, both buttocks and back is pigmented. There are multiple superficial burns of the skin of the right arm, extending from 6 cm. above the elbow to 5 cm. below it on the lateral and flexor surface; on the flexor surface of the right forearm, 4 cm. in diameter; on the left forearm an area, 1 cm. in diameter, 2 cm. above the wrist-joint on the extensor surface, extending 2 cm. upward and inward; and also a smaller, more superficial burn, 5 mm. in diameter. The skin over practically the entire back is involved in superficial burns. . . . The posterior and inner surfaces of both legs, from the upper third of the thigh to 6 cm. below the knee-joint on the left, are involved in superficial burns as well as the anterior surface of the left knee-joint. There are also superficial burns over the external genitalia. There is a debrided wound, partially closed by silkworm sutures and drained by tubes, which extends from the midline (of the back) to the level of the third sacral segment and downward to the left trochanter. The mesial portion of the wound connects with the coccyx, which is fractured. . . ."

"*Organs of the Neck.* The mucous membrane of the trachea and larynx is covered by fibrinopurulent exudate, which is very adherent, appearing as a pseudomembrane. Near the bifurcation of the trachea the mucous membrane is hemorrhagic, with minute ulcerations scattered over the surface.

"Right Lung: The right lung is nodular and crepitant. The pleura is thickened and covered by many firm fibrous adhesions. The cut surface is dark red, moist and studded with irregular round raised areas, reddish in color. From the centers of these areas, yellow, purulent material can be expressed on pressure. Many are soft and necrotic, with a very foul odor.

"Left Lung: The left lung is nodular and crepitant. It is salmon colored and mottled with anthracotic pigment. The lower lobe is covered by shaggy, fibrous adhesions. At the apex of the upper lobe is a firm, grayish, non-aircontaining area, 5 cm. in diameter, which is granular to the feel and on pressure exudes large quantities of yellow purulent material. This area is sharply demarcated from the surrounding tissue. The remainder of the lung corresponds to the

right in description, except that the nodules are fewer in number. The bronchi contain a considerable quantity of frothy bloody fluid. The mucous membrane is markedly injected.

Anatomical Diagnosis. Advanced bilateral bronchopneumonia, with necrosis and abscess formation; acute hemorrhagic, suppurative and ulcerative tracheobronchitis (due to gas inhalation); multiple superficial skin burns; gunshot wound of the left buttock, with compound comminuted fracture of the coccyx; chronic adhesive pleuritis.

"*Probable Cause of Death.* Acute suppurative and ulcerative tracheobronchitis and bronchopneumonia."

CASE IV.—Autopsy 56–68. A. R. M., Private, Co. H., 312 Infantry, No. 3754421. Aged twenty-one years, white. Died January 3, 1919, at 3.45 P.M., at Base Hospital 56. Autopsied January 4, 1919, at 9.30 A.M. First Lieut. George W. Covey, M.C., pathologist.

"*Clinical Data.* This is the case of a man who was admitted to Base Hospital 26 on October 24, 1918, with the history of having been exposed to mustard gas on October 18. There were no skin burns, but the eyes were much inflamed. Examination showed the patient to be quite cyanotic, with marked conjunctivitis, accompanied by purulent discharge and ciliary injection. The pharynx was much injected; pulse good; heart negative; lungs showed many whistling rales throughout, with crackling rales in both bases most marked in the left posteriorly. No definite consolidation. Temperature 102°. October 27, smear negative for B. diphtheria. Dulness and suppression of breath sounds in areas in the right axilla and the right base posteriorly. November 25 he was much improved; still much semipurulent expectoration and cough; chest full of moist and sonorous rales. Heart rapid. Persistent afternoon temperature of 100°. November 30 the throat culture was positive for diphtheria and 10,000 units of diphtheria antitoxin given. He was transferred to Base Hospital 56 on December 1, with very marked membrane on both tonsils. Marked hoarseness. Given 30,000 units of diphtheria antitoxin at 3 P.M. December 3 was given 20,000 units of antitoxin at 9.10 P.M. December 4 the examination of the chest showed marked bronchial breathing all over the lungs, with many rales of all characters. Diagnosis: acute diffuse bronchopneumonia, bilateral, secondary to absorption of mustard gas; diphtheria, pharyngeal and tonsillar. He was given a total of 120,000 units of antitoxin. December 10 the patient had an attack of dyspnea lasting a few minutes. Examination showed respiration of asthmatic type, at the bases a few mucous rales, with areas of consolidation. There was a partial paralysis of the palate. December 17 his condition was about the same; sputum negative for tubercles. December 23 the patient had consolidation of right base of bronchopneumonic type. Quite dyspneic. January 3, 1919, his condition was worse;

unable to take nourishment; bubbling rales throughout lungs. Died at 4 P.M., January 3.

"Pleural Cavities: The left pleural cavity has a strong band of adhesions at the apex. There is no excess of fluid. The right also has a strong band of adhesions at the apex and no increase in fluid.

"Lungs and Organs of Neck: The organs of the neck and the lungs are removed *en masse*. The esophagus is normal. The tonsils, pharynx and upper portion of the larynx are normal. Just below the posterior extremity of each vocal cord there is an opening, about 5 mm. in diameter, leading into a cavity which extends into the laryngeal wall for a distance of about 1 cm. Pus can be expressed from these cavities; otherwise the larynx and upper 5 cm. of the trachea are normal. Beginning about 5 cm. below the larynx and continuing downward throughout the trachea and bronchi the mucosa is dark greenish in color, hemorrhagic and covered with pus. About 5 cm. above the bifurcation there is an ulcer with undermined edges, extending through the mucosa and through a cartilaginous ring to the outer coat of the trachea. It measures 1 cm. in diameter. From this point downward there are similar ulcerations becoming more and more numerous (Fig. 1).

"The left lung is voluminous, heavier than normal. There is a scar at the apex. Numerous hemorrhages are present beneath the pleura. There is marked vesicular emphysema. The cut surface of the upper lobe reveals a group of calcified nodules beneath the scar. The color is normal. Large quantities of pus are expressed from the bronchi and plugs of thick white exudate are expressed from the smaller bronchi and bronchioles. The cut surface of the lower lobe is dark red in color and practically every bronchus contains a plug of exudate which projects above the surface. Frothy bloody fluid exudes from the parenchyma.

"The right lung is heavy, large, firm, with marked vesicular emphysema and numerous hemorrhages beneath the pleura. The pleura is covered by a fibrinopurulent exudate. The cut surfaces of the upper and lower lobes are similar and as follows: Several large, ragged, irregular abscess cavities filled with thin grayish, granular pus, are scattered through the central portions of these lobes from the apex to the base (Fig. 2). They vary from a few millimeters to two or more centimeters in diameter. The central portion of both lobes is an airless, gray, granular mass—a central pneumonia. Toward the pleura the pneumonic areas become more discrete and are seen as gray, raised, granular areas varying from 3 or 4 mm. to 1 cm. or more in diameter, quite definitely circumscribed. In the center of each is a bronchiole from which a plug of exudate can be expressed. Occasionally the center of a larger discrete area is seen to be necrotic, with a small abscess cavity (Figs. 1 and 2). The parenchyma intervening between the pneumonic areas is dark red in color and emphysematous, with areas of

hemorrhage. Near the hilus are scattered areas showing interlacing, firm yellowish streaks suggesting organization.

"*Anatomical Diagnosis.* Marked gangrenous and ulcerative tracheobronchitis; marked fibrinopurulent bronchitis of smaller bronchi; massive bronchopneumonia, right, with extensive necrosis and abscess formation; healed pulmonary tuberculosis; right-sided fibrinopurulent pleuritis; chronic adhesive pleuritis; marked vesicular emphysema.

FIG. 1.—Larynx and trachea two months and ten days after gassing (Aut. 55–68, Case IV in text). Note extensive ulcerations, most marked at the bifurcation. The large transversely placed ulcer in the lower part of the trachea perforated through a cartilaginous ring.

"*Probable Cause of Death.* Gangrenous and ulcerative tracheobronchitis; bronchopneumonia, with abscess formation—following inhalation of poisonous gases."

Microscopic Study (Slide 449). The striking feature of the section is a small bronchus dilated and filled with pus cells. In the center of this mass is a group of vegetable cells and spirals. The wall of

the bronchus is only faintly visible, being infiltrated with polymorphonuclear leukocytes. The mucosa is entirely absent. The capillaries are intensely injected and dilated. In two places the wall is completely necrosed, and this necrosis extends for some distance into the parenchyma of the lung. About the bronchus and throughout the section there is thickening of the alveolar walls, which are infiltrated with polymorphonuclears and show a large increase of connective tissue. The alveoli are filled with fibrin and heavy

FIG. 2.—Lung from same case as Fig. 1. (The trachea and larynx are lying back of the lung, with the epiglottis and base of tongue showing just beneath the base of lung). Note the numerous areas of consolidation scattered throughout the cut surfaces. In the centers of many of these the emptied lumina of the bronchioles may be seen. Note the ragged areas of necrosis and abscess cavities.

precipitated serum through which are scattered a few cells. Fibroblasts are seen penetrating the exudate in numerous instances, and some alveoli are completely fibrosed.

DISCUSSION. Case I died the day after admission, and, allowing one day for transportation from the field, about five days after

gassing. Here are seen, as the outstanding features, edema, congestion, hemorrhages and very small ulcerations, with thin fibrinopurulent exudate in the upper respiratory tract. In the lower air passages one finds much the same picture with a more tenacious exudate which almost completely plugs many bronchioles. The parenchyma shows congestion, edema, emphysema, areas of atelectasis and very small bronchopneumonic areas.

FIG. 3.—Larynx and trachea from a case of mustard-gas inhalation. Note extensive edema of aryepiglottic folds especially the right; thick, shaggy membrane covering the larynx and vocal cords; membrane in patches on the wall of the trachea and bronchi; small ulceration of the wall near the bifurcation.

Case II died about six days after gassing. The exudate in this case is much more abundant than in Case I, and is shaggy and membranous. The ulcers in the trachea are a little more prominent. There is already a pleurisy present.

Case III died twenty days after gassing. The air passages show a marked pseudomembrane, and, upon its removal, a hemorrhagic and ulcerated surface. The lungs showed an advanced broncho-

pneumonia, with beginning necrosis and abscess formation in the center of some of the pneumonic areas.

Case IV died two months and ten days after being gassed. The air passages, trachea and bronchi show no membrane, but instead show marked necrosis of the mucosa, with large, deep ulcerations extending nearly through the tracheal wall. The lungs show extensive necrosis and abscess formation, accompanying a massive

FIG. 4.—Larynx and trachea from case of mustard-gas inhalation. Note thick membrane covering epiglottis, obscuring the vocal cords and extending in patches down the trachea; thick membrane on the walls of the primary bronchi; small ulcerations of tracheal wall near the bifurcation.

bronchopneumonia. The attempt at healing is shown by the organization of the exudate. Many alveolar walls are thickened and some alveoli are completely fibrosed. Strange to say, much albuminous deposit and fibrin are still in evidence in the air cells. Unfortunately, this case was complicated by clinical diphtheria, but most probably this complication did not materially change the lesions found at autopsy. Only one finding brings up a question of etiology: the evidences of the aspiration pneumonia as revealed by food particles lying imbedded in the purulent exudate within the small radicles of the bronchi. Was the aspiration of the material due to the par-

alysis following the diphtheria or to the deep ulcers in the trachea opposite the esophagus? The abscess formation might also have been augmented by the aspiration of the foreign material.

To recapitulate: Stage one, as represented by the first two cases, is characterized by mild edema, hemorrhage, beginning ulceration, early fibrinous deposit, emphysema and very early bronchopneumonia. Stage two (Case III) by a marked fibrinopurulent pseudomembrane, more extensive ulceration, emphysema, advanced bronchopneumonia and beginning necrosis. Stage three (Case IV) by ulceration, necrosis and abscess formation, with massive bronchopneumonia. The attempts at healing are revealed by the organization and fibrosis.

It is interesting to speculate on the outcome of a case similar to the fourth should such a case go on to recovery or if the lesions in the trachea should continue to progress. The tracheal ulcerations might easily perforate the wall, resulting in mediastinal abscess. Those in the bronchi near the bifurcation might ulcerate through and through and perforate the aorta. When such ulcers heal, contractures are sure to obtain. These contractures may result in traction diverticulæ of the esophagus. In the parenchyma, organization would occur and result in disseminated patches of fibrosis or even in extensive fibrosis of the lungs resembling healed tuberculous lesions. Some of the bronchioles might be transformed into fibrous cords through the organization of the exudate.

In milder involvement the walls only might go on to a fibrosis of a greater or lesser degree, which would result clinically in a chronic bronchitis. Upon the extent of the injury to the bronchial tree will depend the intensity of the clinical symptoms of convalescent and recovered cases, as manifested by the chronic bronchitis and emphysema. From what has been said above, many cases will undoubtedly present grave clinical difficulties in the differential diagnosis from pulmonary tuberculosis.

CLIMACTERIC HYPERTENSION: A STUDY OF HIGH BLOOD-PRESSURE DURING AND FOLLOWING THE MENOPAUSE.

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In this paper it is my purpose to describe a type of high blood-pressure developing in women at the time of the menopause and possibly the result of it, in which there is no discernible arteriosclerosis, at least, for some years after its onset, no renal involve-

ment and frequently no symptoms of any kind for possibly a decade or longer. In the early stages it is usually overlooked unless some intercurrent disease develops, and thus invites a thorough examination of an otherwise apparent healthy woman. Occasional references have been made in the literature on hypertension to a type occurring in women at the climacteric, but beyond noting the existence of such instances but little has been written.

Clifford Allbutt,[1] in 1903, against the then prevailing opinion that hypertension was always secondary to arteriosclerosis or nephritis, called attention to the fact that the hypertension in a certain proportion of cases was primary and the sclerosis secondary.

In 1914 Stengel,[2] writing on cardiorenal disease, noted cases of primary arterial or arteriolar disease, the onset and early course of which were so insidious that the history furnished little clue to the nature of the disease.

Arteriocapillary fibrosis as described by Gull and Sutton was at that time accepted as adequate to explain many cases of this type of cardiorenal disease, though in these days too much stress is laid upon renal disease as being the constant source of hypertension and of arteriosclerosis. Stengel referred to the frequency of hypertensive cases in which there was "considerable diffuse arterial thickening" (hard vessel walls, increased substernal dulness, ophthalmic findings), and the symptoms of which were almost wholly those of hypertensive cardiac involvement. He noted the occurrence of these cases in persons from forty to fifty years of age, and a greater frequency in women than in men. The patients were robust, with normal blood pictures and normal renal functional tests, the urinary examinations showing traces of albumin and hyaline casts. The high pressure and cardiac embarrassment were the most impressive facts. Thus on good grounds he separated these cases from primary renal disease.

Again, in 1915, Allbutt,[3] in a monograph, described a condition the essential feature and earliest manifestation of which was hyperpiesia or elevated blood-pressure. This has been termed "benign," "essential" or "primary" hypertension, and coincides with Janeway's "chronic hypertensive cardiovascular disease." Two years later Stengel,[4] in a paper on the "Classification of Chronic Nephritis and the Relation of Infection to Kidney Disease," further clarified the situation by a clear-cut classification of chronic nephritis in which he described "renal sclerosis" as falling into four possible forms, *i.e.*:

1. Primary sclerosis following acute interstitial nephritis.
2. Secondary sclerosis following glomerulonephritis or mixed forms of nephritis.

[1] Rise in Blood-pressure in Later Life, Med. Chir. Soc., 1903, lxxxvi.
[2] Cardiorenal Disease, Jour. Am. Med. Assn., October 24, 1914, lxiii, 1463–1467.
[3] Diseases of the Arteries, Including Angina Pectoris, 1915.
[4] The Classification of Chronic Nephritis and the Relation of Infection to Kidney Disease, Med. Clin. of North America, September, 1917, p. 217.

3. The terminal sclerotic kidney following arteriolar sclerosis.
4. The atrophic kidney of senile arteriosclerosis.

Stress was laid particularly on the third form, *i. e.*, the form following arteriolar sclerosis, in which the symptoms are not nephritic and the kidney condition and function remained unimpaired for long periods of time. As in his former paper, he noted the healthy appearance of these individuals and the frequency in which the patient was unaware of any illness. Marked changes in the retinal arterioles and sometimes retinal hemorrhages occurred in these cases. Of further interest he noted the rapid recovery of a man with elevated blood-pressure, albumin and casts, etc., after the cleaning up of pus pockets at the roots of the teeth.

Meara,[5] a year later, presented a series of his own cases, with a general discussion of essential hypertension. He also noted the occurrence of the disease in ruddy, stocky patients with *plethoric habits, active temperament*, live *men* and *women*. He describes them as gourmets if not gourmands, and emphasizes the influence of overeating as a causative factor.

The point which I wish particularly to emphasize from the study of my series of 51 cases of this type is the characteristic development of a type of hypertension in women, with its onset at the menopause or soon after, in which there is little if any evidence of fibrosis of the peripheral vessels, at least, for some years after the onset. The past medical histories in the cases I have selected are strikingly lacking in any of the predisposing or exciting causes of renal sclerosis or chronic nephritis, and this is in marked contrast to many of the cases presented by Meara, who includes a number of male patients. In both his male and female patients there are noticeably present some one or more infections in the past history or even of former attacks of nephritis. In his cases there was frequently a moderate retention of blood-urea nitrogen and at times some reduction in the phthalein. In short, the cases described by both Stengel and Meara would seem to fall well within the group of "renal sclerosis" and the subgroup renal sclerosis following arteriolar sclerosis, but undoubtedly include patients who could be placed in the group which I have selected from several hundred cases of hypertension, and which will now be described.

As mentioned above, the condition is, at times, discovered during the menopause, and at this time it has as its only indication a definite rise in both systolic and diastolic blood-pressure. The height of the pressure was in many of the cases very marked, running up to systolic 230–250–310 and diastolic 130–140–150. On the other hand, in the cases examined early in the course of the disease, pressures as low as systolic 180–190 and diastolic 100–110 were found. Rarely were lower figures noted, the higher ones being the rule.

[5] Hyperpiesia of Clifford Allbutt, Med. Clin. of North America, July, 1918, p. 1.

As it is at present these cases are frequently discovered in the course of a routine physical examination which has been prompted by some intercurrent disturbance or disease or at the time of a life insurance examination. Unfortunately, they are more frequently discovered several years after the menopause, when, following an indefinite period of vague symptoms, nervous, gastric or cardiac, the patient seeks relief and is surprised to know that her blood-pressure is high, and, by then, even very high. The majority of the cases fall within office rather than hospital practice, and possibly for this reason the literature on the subject is incomplete. Their appearance is strikingly healthy and their weight usually above the average; frequently they are obese. These women, usually from the upper social strata, are energetic, active and inclined to be of an intensely nervous temperament, used to good living and fond of life, but, nevertheless, subject to many worries and anxieties for years, as may be elicited in their histories.

The majority are discovered between the ages of fifty and sixty years, and it is toward sixty years, for the first time, that slight fibrosis of the peripheral vessels is noted, and during this period changes in the retinal arterioles make their appearance and thus occasionally an examination by the ophthalmologist may first reveal the condition.

Of the chief symptoms prompting the patient to consult medical advice, the gastric and nervous groups are the most common, the symptoms falling within the gastric neurosis group, with fermentation and constipation in marked evidence. Then nervousness and pains, chiefly in the limbs, were equally frequent. Headache and evidences of cardiac embarrassment come next in frequency, with finally a few cases complaining of weakness, vertigo, epistaxis, etc. However, headache was present in varying degrees in nearly all patients.

Contrasting this group of complaints with that of a group of renal sclerosis cases, with hypertension occurring in men between the ages of fifty and sixty years, I found that cardiac embarrassment and pain in the limbs had a decided preponderance over all other symptoms, and of equal importance in this differentiation is the fact that the peripheral vessels of the men patients were all markedly sclerosed in contrast to those of the women. Not only was there the difference of sclerosis in peripheral vessels, but also in the retinal arterioles which were involved, as a rule, in the male cases, regardless of age, while in the women the retinal sclerosis occurred in only two groups, the first group being those approaching sixty years or past and the second being represented by the occasional case in which there was a past history of scarlet fever, pneumonia, etc., or in which there was a local focus of infection as cryptic tonsils or diseased roots of teeth.

On the other hand the past medical histories of the men were rich

in the recognized causes of arteriosclerosis and nephritis, as rheumatism, pneumonia, scarlet fever, syphilis, typhoid, lead, alcohol and finally local foci of infection, almost all of which conditions were lacking in the histories of the women patients.

The blood picture again showed a distinct contrast, for of the male cases all but one were below the normal limit, while of the women it was the exception to find anemia, and when it did exist there was present some other disease which could readily account for it.

The contrast of the two groups is further noted in the urine analyses and the renal functional tests. In the renal sclerosis of male cases the urine contained a cloud or heavy trace of albumin and many hyaline and granular casts, the phthalein was considerably impaired and the blood-urea nitrogen slightly increased. On the other hand the cases in women showed, as a rule, but a faint trace of albumin, with hyaline casts in a few instances. The phthalein was impaired only when cardiac weakness had developed and the blood-urea nitrogen remained normal throughout. It was also normal even during periods of forced proteid feeding (Hopkins and Jonas[6]). There was quite a variation in the specific gravity of morning and evening samples in both groups.

I could cite other points of contrast in my endeavor to differentiate between these two types of hypertension, but I believe the above points are adequate to substantiate the differentiation, and to place, as a distinct entity, the hypertension of the menopause, which one might style endocrinal hypertension.

So far as I have been able to elicit from this survey of several hundred hypertension cases the true type of what has been called "benign" or "essential" hypertension, *i. e.*, hypertension without arterial or arteriolar sclerosis, is to be found only in women at or following the menopause. It may exist for a number of years without any distinguishable sclerosis, but in later years, *i. e.*, as a rule, from fifty-five to sixty years, sclerosis tends to develop and the ultimate termination is either a cerebral hemorrhage or a cardiac death. Throughout its course there is no evidence of kidney disease.

A brief presentation of a few typical cases may be of interest:

Case I.—Miss M., aged fifty years, was admitted to the University Hospital owing to attacks of vomiting and weakness. She had never been ill before the onset of the above symptoms, which developed along with evidences of the menopause. She had been subject to many worries for years. Naturally of a nervous temperament, the nervousness had become aggravated with the onset of the attacks of nausea and vomiting. Palpitation was troublesome at times. She was chronically constipated. Physical examination revealed the following: Blood-pressure: systolic, 245; diastolic,

[6] Studies in Renal Function, with Special Reference to Non-protein Nitrogen and Sugar Concentration in the Blood, Phenolsulphonephthalein Elimination and Blood-pressure, Arch. of Int. Med., June, 1915, xv, 964–973.

125. Slight exophthalmos; thyroid enlarged. The heart was enlarged to the left and there was a slight systolic murmur at the mitral area, with accentuation of the aortic second sound. No peripheral sclerosis, and the eye-grounds were negative. The urine showed a specific gravity of 1017, there being neither albumin nor casts. Renal functional tests were also negative; phthalein elimination 70 per cent., and the blood-urea nitrogen 12 mg.

With rest and treatment the pressure fell to systolic, 170; diastolic, 90; and the patient became very much improved.

CASE II.—Miss P., aged forty-nine years, complained on admission of pains in the lower limbs. She had always been healthy aside from one attack of influenza and tonsillitis, and at twenty-nine years an exophthalmic goitre of several months' duration. Her menopause occurred nine years ago. She had been subject to hard work and many worries for years. Her present trouble she dates back two years, recurrent attacks of pain down the lower limbs being the chief complaint. Dyspnea on exertion and slight edema of ankles were noted on admission, and at times she was subject to headache.

Physical Examination: General appearance robust and obese (weight, 187 pounds). Blood-pressure: systolic, 195; diastolic, 120. Blood picture normal. Cardiac outline increased slightly to the left. Accentuation of aortic and pulmonic second sounds. No peripheral sclerosis, and the eye-grounds were normal. The urine showed a specific gravity of 1015, with neither albumin nor casts, and the phthalein elimination was 55 per cent.

Here again after treatment the pressure fell to systolic, 145; diastolic, 75, and there was marked improvement in the patient's condition.

These two hospital cases present interesting features in that their past histories were quite as negative as that of the average normal woman of their age. They had both been subject to nervous strain for years. In one the symptoms developed with the menopause and in the other not for several years later. In one the thyroid was enlarged and in the other there was the history of exophthalmic goitre in the past.

Peripheral and retinal arteriolar fibrosis were absent in both and renal function was normal.

CASE III.—Miss C. S., aged fifty-three years, first consulted me a year ago, complaining of stomach trouble. For four years prior to that she had been subject to intense nervousness, nausea, fermentation and constipation. She was also troubled with numbness and tingling in the limbs. All these symptoms developed with the onset of the menopause. She had been subject to worries for years. Her past medical history was negative aside from an attack of tonsillitis years ago.

Physical examination revealed the following: Well-nourished—

in fact, rather obese—woman, apparently in good health. Blood-pressure: systolic, 235; diastolic, 130. Blood picture normal, cardiac outline normal, systolic murmur at aortic and mitral areas with accentuation of aortic second sound. No evidence of fibrosis of peripheral or retinal vessels. The urine showed a specific gravity of 1025 and a trace of albumin but no casts.

CASE IV.—Miss A. M., aged fifty years, consulted me about two years ago, complaining of fatigue and nervousness, both of which she had noticed in varying degrees for four years, during which time and preceding it for three years she was troubled with hot flushes and menstrual irregularities. She was also subject to vague pains in the back. Her past medical history was negative.

Physical examination revealed a very robust, healthy looking woman. Blood-pressure: systolic, 250; diastolic, 140. Blood picture normal. No apparent increase in cardiac outline. Slight systolic whiff at the aortic and mitral areas, with accentuation of the aortic second sound. No evidence of peripheral or retinal arteriolar changes. The urine showed a specific gravity varying from 1011 to 1018, with a slight trace of albumin and no casts. Phthalein elimination, 82 per cent.

Under treatment her blood-pressure was readily controlled, though fatigue or excitement produced marked rises.

The last two cases are very typical of the office group, both occurring in patients of the better class and of the high-strung, intense, nervous type, and finally both being robust and without evidence of renal involvement or vascular changes.

Now in contrast it may be well to cite one of eleven cases kindly furnished me by Dr. Stengel, which would seem to illustrate the influence of gout on the vascular system, with possibly the superimposed influence of the absence of ovarian secretion and its consequent results.

CASE V.—Mrs. Y., aged sixty-one years, complained of pain and swelling of joints for the past five years. She was subject to headache, vertigo, palpitation, dyspnea and edema. Her past medical history was negative, aside from recurring attacks of gout and an operation for the removal of both ovaries, sixteen years ago, for a uterine tumor.

Physical examination revealed a well-nourished woman with very evident gouty changes in her joints. Blood-pressure: systolic, 310; diastolic, 160. Peripheral vessels markedly sclerosed and advanced arterial changes in the retina. The urine showed a specific gravity varying from 1007 to 1036, with a trace of albumin and an occasional hyaline cast. Phthalein elimination, 64 per cent. This case falls within the so-called hyperpiesia group or Janeway's cardiovascular group, but the advanced sclerosis and the past and present history of gout would readily exclude it from the group of menopausal hypertension cases above described.

The influence of castration in the occasional case in this series is interesting, but my data concerning it is, so far, too inadequate to permit of an expression of opinion.

Now, by way of contrast, I will go one step farther by citing two male cases, which by Allbutt and Meara would be classed under benign or essential hypertension, but which should be classified, I believe, in Stengel's group of renal sclerosis or the group of arteriolar fibrosis of Gull and Sutton.

CASE VI.—Mr. H., aged fifty-seven years, entered the University Hospital complaining of dyspnea and epigastric pain. These symptoms developed five months before, and gradually he noted vague pains in the limbs, palpitation, edema and constipation. His past medical history included scarlet fever, measles, gout, syphilis, Neisserian infection and the abuse of alcohol.

Physical examination revealed a well-nourished male of 170 pounds weight. Pus pockets at roots of the teeth. Blood-pressure: systolic, 175; diastolic, 130. Hemoglobin, 85 per cent. Cardiac area enlarged and heart sounds weak. Marked sclerotic changes in peripheral vessels. Wassermann reaction negative. The urine showed a specific gravity of 1010, with a trace of albumin and hyaline and granular casts. Blood-urea nitrogen 27 mg. and phthalein elimination 45 per cent.

Is there not sufficient cause for renal damage in this man's past history? The blood-urea nitrogen is only very moderately increased and the phthalein moderately reduced, but in spite of quite fair renal function it would seem inevitable that the fibrosis should have involved the renal vessels to a fairly marked degree.

To select another illustration from the group of male cases:

CASE VII.—Mr. G., aged fifty-four years, was admitted to the University Hospital in an unconscious condition. Prior to this sudden attack of unconsciousness he had noticed some weakness and occasional blurring of vision, but no other symptoms. His past medical history included repeated attacks of acute rheumatic fever and the abuse of alcohol, besides having done heavy physical work for years.

Physical examination revealed a male of medium build. Blood-pressure: systolic, 195; diastolic, 110. Hemoglobin, 70 per cent. Pus pockets at roots of several teeth. Cardiac area enlarged and muscle tone poor. Peripheral and retinal arteriolar sclerosis advanced. The urine showed a specific gravity of 1013, with a cloud of albumin and many hyaline and granular casts. Blood-urea nitrogen 20 mg. and phthalein elimination 50 per cent. Here, as in the above case (No. VI), we have marked fibrosis of the vessels, albumin and casts in abundance, yet fair renal functional tests. But here also, as above, the past medical history contains sufficient evidence to account for the general sclerotic changes and probably renal changes as well. Besides the histories, both patients had

faulty dental conditions, which could in themselves furnish a local source of intoxication and contribute to the condition.

These cases, I think, illustrate clearly the contrast between arteriolar disease, with probable renal sclerotic changes on the one hand, and on the other the menopausal hypertension group, which seems to be in a class alone, and which, to me, represents the only true type of "benign" hypertension.

How correct the term "benign" is I question when I look back over the records of these patients for several years. They usually do well under treatment, but their desire to overdo and their naturally nervous temperament are their worst enemies.

ETIOLOGY. The etiology of this condition will bear investigation. I have shown above that these cases are usually free from the causative factors of arteriosclerosis and nephritis as accepted today. Overeating, as suggested by Allbutt, may be and probably is a contributing cause of "hyperpiesia," accepting that term in the sense in which he used it. I cannot see that it has been a contributing cause in this series of menopausal hypertensive cases.

Mental strain and worry and a naturally nervous temperament when superimposed on the profound emotional and bodily changes occurring at the time of the menopause would seem to be more naturally provocative of the trouble. Marriage and child-bearing seem to play no part, as many of the cases were single, and of the married, some had children and others had not.

To consider then the influence of the menopause on the production of this type of hypertension, certain established facts must be presented in support of this theory.

"The ductless glands by their correlation form a perfect physiological balance which is preserved by a proper distribution of harmony and antagonism between the functions of the various glands.

"If one of the glands is diseased or extirpated the normal balance is upset and the organism of the individual may be affected by the abnormal action of one or more distant glands of the group."

In considering the glands of internal secretion, I wish particularly to call attention to the adrenals, pituitary body, thyroid and ovaries.

The medulla of the suprarenal system elaborates the hormone adrenalin which influences the sympathetic nervous system, blood-pressure, the distribution of blood and the tonus of organs innervated by the sympathetic system. This hormone of the chromaffin system is in turn greatly influenced by conditions of emotional disturbance and certainly during the menopause, in some cases, the emotional disturbances are profound. The relation of the suprarenal system to the glands of sex is illustrated by the cortex, lipoid granules being present in it, just as they are in the interstitial and luetal cells of the ovary. Furthermore, the cortex enlarges during breeding and pregnancy (Vincent[7]).

[7] The Experimental and Clinical Evidence as to the Influence Exerted by the Adrenal Bodies upon the Genital System, Surg., Gynec. and Obst., September, 1917, xxv, 294.

Functional activity of the hypophysis is closely related to that of the sex glands, extracts of the anterior lobe having a distinct influence on the sexual apparatus, and the gland enlarging during pregnancy. Of further interest bearing on this subject of hypertension, extracts of the posterior lobe when administered clinically produce an elevation in blood-pressure.

"The ovary is recognized as a true organ of internal secretion. The corpus luteum in its full development presents the characteristic picture of an internal secretory gland. It develops at the age of puberty, and coincident with this is the appearance of the cyclical changes of menstruation, which changes disappear after the cessation of the corpus luteum formation at the climacteric. The atretic follicles are believed to be the further source of internal secretion of the ovary, the absence of the corpus luteum being sufficient evidence that there is some other portion of the ovary used for the primary source of the secretion. There is much to show that the action of the ovarian secretion is neither direct nor selective, but that it exerts only a balancing influence on other correlated and more powerful glands, the activity of which the ovarian secretion discharges or suppresses as the case may be. With the hypofunction of this gland we have not only to consider the effects of diminished secretory power, but also the changes wrought in the other members of the group, the balance of whose function has thus been disturbed.

Furthermore, the influence of castration after maturity has led to variations in sugar assimilation, coagulation time of the blood and chemical composition of the blood, as well as a tendency to adiposity.

"Variations in the size of the thyroid gland during certain phases of the female sexual life have been recognized for years. Marked enlargement at puberty, with associated palpitation and evidences of vasomotor disturbances, are attributed to a hypersecretion of the gland at this period. Early extirpation of the thyroid not only produces degenerative changes in the ovaries, but delays the time of puberty and limits the productivity of the individual, and, further, women with diseased thyroids usually have menstrual disorders.

"An interesting observation of Lange is that women in whom the thyroid does not swell exhibit a renal albuminuria, and he expresses the belief that the swelling of the thyroid acts as a protection against certain poisons which are set free as a result of pregnancy, and which, without the protection of the secretion from the hypertrophied thyroid, are injurious to the kidneys" (Graves[8]).

Several instances of exophthalmic goitre have occurred at the climacteric and have led to the suggestion that the neuropathic and vasomotor symptoms of the change of life are the result of hyperactivity of the thyroid gland.

Illustrative of the effect on the endocrine glands of emotional

[8] Gynecology, 1918.

stress are the results of Etinne and Richard,[9] who observed several patients who had been in Nancy during repeated violent bombardment from big guns and aëroplanes. They cite the development of exophthalmic goitre in an acute form, with high blood-pressure in two women of twenty-four and thirty-four years. They also noted that in some women menstruation was arrested by the bombardments. In one man Addison's disease appeared and was followed by the symptoms of exophthalmic goitre, and in two other instances Addison's disease became superimposed on preëxisting exophthalmic goitre.

These cases are especially interesting in that they show exophthalmic goitre of emotional origin may develop with suprarenal hyperfunctioning as well as with hypofunctioning, and, further, that the suprarenal trouble may also become superimposed on exophthalmic goitre.

The correlation of these glands I have dealt with at some length, noting the more important recent clinical and experimental evidence, with the intention of presenting, as the possible cause of menopausal hypertension, a disturbance in their functioning. As mentioned above the disease is lacking in any other clear-cut etiological factor.

At the menopause, with the withdrawal of at least a part of the internal secretion of the ovary from its place in the connecting link of endocrine glands, it would be a natural assumption to consider that a certain amount of depressor influence of the ovary was withdrawn from the adrenals, hypophysis and thyroid, leaving them, as it were, out of balance.

Knowing that there are produced in one or more of these glands substances that increase blood-pressure, influence the sympathetic nervous system (vasomotor system) and the sex glands, aid in regulating metabolism, and, finally, exhibit an intimate relationship with emotional disturbances, it does not seem improbable that the blood-pressure is, by a combination of these altered influences, raised and sustained at a high level. A persistently high pressure of this type will, in the course of years, produce fibrosis of the vessels, and this we have seen develops in the latter years of these patients, though I have known them in a few instances to reach sixty years and over without the slightest evidence of peripheral or retinal sclerosis. If a routine blood-pressure were taken of all women at the menopause I believe the results would be of great diagnostic and therapeutic benefit for the patients' future.

NOTE.—Prognosis and Treatment will be given in a later paper.

[9] Exophthalmic Goitre and the Bombardments, Bull. de la Soc. méd. des Hôp., Paris, December 20, 1918, No. 36, xlii, 1196.

REVIEWS

SURGERY OF THE SPINE AND SPINAL CORD. By CHARLES H. FRAZIER, M.D., Professor of Clinical Surgery in the University of Pennsylvania. Pp. 909; 378 illustrations in the text. New York and London: D. Appleton and Company.

THE appearance of this large volume limited to the field of the spine and spinal cord by a master of the subject is an event of importance to the great army of surgeons who cannot hope to attain special experience and knowledge in this branch of surgery. To the ordinary surgeon who cannot keep abreast of the literature of this and other fields of general surgery, the only available guidance comes from text-books and systems of surgery. It was the author's purpose to discuss the conditions so comprehensively that it would not be necessary for the reader to consult collateral works. To this end special authorities have contributed chapters on anatomy, normal and pathological physiology, cerebrospinal fluid and its relations to spinal diseases and on the roentgen-ray examination. Piersol devotes 96 pages to a detailed discussion of the anatomy, including its histological and embryological aspects, and lays a strong foundation which is very important. Allen covered the normal and pathological physiology thoroughly and interestingly. The part played by the cerebrospinal fluid in spinal surgery, as brought out by Kolmer will be of great value to most surgeons because such information is usually not readily available to them. Pancoast's presentation of the roentgen-ray examination of the spine is replete with excellent roentgen-ray illustrations and valuable points drawn from his long and rich experience.

The purely clinical aspects of the whole field are discussed by Frazier in the remaining portion of the book, about 650 pages. He devotes special chapters to spina bifida, trauma (chiefly sprains, dislocations and fractures, and their complications), stab and gunshot wounds, tumors and meningitis. Other chapters are given to surgery of the spinal roots, rhizotomy, lumbar puncture, intraspinal therapy, spinal anesthesia, laminectomy, chordotomy and decompressive laminectomy.

The special appeal of the volume to most surgeons will come from the author's rich experience and intimate knowledge on subjects the average surgeon knows little about because he rarely meets

with them and because the sum total of available information is not particularly great. He may now have at his easy disposal a well digested resumé of the most advanced thought on each of the subjects discussed, with a wealth of excellent illustrations. It is something he has long felt the need of and he will surely take advantage of the opportunity now afforded to have this volume within easy reach when the need again arises. T. T. T.

DISEASES OF THE HEART AND BLOODVESSELS. By THOMAS E. SATTERTHWAITE, A.B., M.D., LL.D., Sc.D. Pp. 328; 42 illustrations. New York: Lemcke & Buechner.

THIS work, with a chapter by Dr. W. Wayne Babcock, of Philadelphia, on cardiac surgery represents to a great extent, a compilation, with revision, of the various publications of the author. In general the chapter arrangement meets with our approval, but we, although acknowledging the thoroughness of Satterthwaite's methods, scarcely recognize as so important in a book of this kind the chapter on cardiac parasites and Graves's disease. There are many good points in the book which overbalance some features to which the reviewer may take exception. The author in one place makes the observation that diastolic pressure readings will be inaccurate "if the examiner's hearing is defective" and if the patient's general circulation is poor, and on this account he remarks that life insurance examiners are not expected to give special weight to diastolic readings. In another place he emphasizes how easy diastolic pressures may be read and how important the estimations are. Deafness in a physician can scarcely be a sufficient cause for discouraging the taking of diastolic pressure. Satterthwaite believes diabetes and Graves's disease are associated with hypotension, with which statement the reviewer takes issue. Also, we find that all intestinal toxemias have hypotension (p. 68); yet, on page 70, when he skims over the management of hypertension he recommends certain things to combat intestinal toxemia in order to reduce hypertension.

He says endocardial murmurs are of two kinds, organic and functional, the former heard "when there is a mechanical hindrance to the flow of the blood from ulcerations, etc., of the valve." What of the regurgitant murmurs? We do not like this sentence. "The right ventricle gets to be hypertrophied" (p. 98). We find no mention of the Graham Steell murmur in Mitral Stenosis, although we believe this valve lesion is otherwise well described. On page 116 an American author is given the credit for emphasizing the difference between arm and leg pressure in aortic disease, but if

reference is to be made to this important phenomenon, why not refer to Leonard Hill? Also, we find no mention of increase of pulse-pressure in aortic insufficiency, although pulse-pressures (p. 18) are said to be very important. On page 152, the revival of a man by the pulmotor four hours after his heart had ceased to beat, is quoted, but why and wherefore? Strange things have occurred in medicine, but not that!

The reviewer having had charge of cardiovascular examinations in the Army was charmed by this paragraph: "In the examination of recruits it is important that the man examined should not be allowed to remain long standing prior to his examination. The quarters should also be warm and agreeable and the examiner cheerful and not abrupt in his methods." "'Tis a consummation devoutly to be wished," but, we fear, in this cardiovascular boards failed signally and never attained the beautiful ideality described by Satterthwaite.

There are more minor and major points in the book which may be criticized, among them incorrect spelling of proper names; but it is time to praise. Apart from the undoubted impression which the reviewer received from the book, to wit, that it was prepared hastily, there is much of value therein. The description of electrocardiograms and other polygrams is good, also arrhythmia, and the illustrations, mainly by the author, are good, although there is a mistake in numbering, which is confusing. On page 180 there is Fig. 41 and on page 246 Fig. 86, but what has become of the intermediate figures? We could find none.

Although commendable, we must repeat, the book seems to us to have escaped the drudgery of revision and to have suffered from having escaped. The chapter by Dr. Babcock on surgery of the heart is a good and concise compilation, but it may be questioned whether such a chapter, however valuable in a comprehensive treatise, has a place in a volume from which much of importance has been omitted in order to the reduce the size of the book.

E. H. G.

PHYSICAL AND OCCUPATIONAL REËDUCATION OF THE MAIMED. By JEAN CAMUS. Pp. 195; 64 illustrations. New York: William Wood & Co., 1919.

THIS book has left the reviewer with the impression that too much has been crowded into a few pages, hence the feeling that only the surface has been scratched. One point has been emphasized, and that is the futility of all reconstruction work unless the disabled man puts his heart into his treatment. Not only physical reconstruction is needed, but psychic reconstruction as well. Having

been in several general hospitals where such work is being carried on, the reviewer has been, indeed, impressed with the difficulties surrounding the reconstruction of a man who does not desire to be reconstructed and the insidious permeation of this man's attitude among those who are eager to be benefited. Illustrations add much to the text of Camus's book, which has been ably translated by W. F. Castle. Articles on British institutions have been contributed by British authorities, including Sir Arthur Pearson. Mechanical appliances are described, and the several occupations a maimed man can be trained to fill are well discussed. E. H. G.

QUARTERLY MEDICAL CLINICS. By FRANK SMITHIES, M.D., at Augustana Hospital, Chicago. Vol. I, No. 1 Pp. 188; 42 illustrations. St. Louis, Mo.: Medicine and Surgery Publishing Company, 1919.

WHAT may be termed the "Chicago Idea" of publishing for general information the work of the clinics of that city is augmented by this volume from the prolific pen of Dr. Smithies. The reviewer has found the *Quarterly Medical Clinics*, which is described as "A Series of Consecutive Clinical Demonstrations and Lectures," a very successful record of the clinics and lectures given to the senior students of the University of Illinois.

We have no doubt of the future success of Smithies's undertaking if this first volume is a sample of the works which will follow quarterly. The subjects have been well selected, the exposition of the cases has been carefully written and the deductions on which the ultimate diagnosis and treatment have been based are logical and consecutive. Not only senior students but medical practitioners as well should find much of value in this new volume from Chicago.
E. H. G.

THE HUMANE SOCIETY OF THE COMMONWEALTH OF MASSACHUSETTS: AN HISTORICAL REVIEW, 1785–1916. By M. H. DE WOLFE HOWE. Pp. 398. Illustrated. Boston: Riverside Press.

IT is a pleasure, and may we say a relief, to turn from purely medical literature to the perusal of a book which makes its appeal to the general public rather than to the medical profession, for in this book we are told interesting things of how the Humane Society was formed to prevent the bugbear of those days, premature burial; of ancient methods of reviving those apparently dead; of the rewards given to the person who shall first discover and endeavor to recover the subject; of the development of life-saving at sea; of the

founding of the Massachusetts General Hospital! What a controversy took place over placing a drowned child in bed between two penrsons of good constitution, as the "salutary effects of the natural vital warmth have been clearly proved in a variety of successful cases!" What a discussion about the value of blowing tobacco smoke into the bowel! And we may imagine the storm aroused by the recommendation not to bleed those supposedly dead!

Engravings, profuse and beautiful, illustrate the text. Original documents are reprinted, original odes and poems, noteworthy for their purport, not for their poetic value, quaint in their thought, ponderous in their expression, all add to the enjoyment of Howe's splendid production. From the standpoint of the historian the work is invaluable; as a picture of the noble activities of a group of early humanitarians it is irreproachable; that it is an interesting book is undeniable. E. H. G.

GILBERTUS ANGLICUS MEDICINE OF THE THIRTEENTH CENTURY. By HENRY E. HANDERSON, A.M., M.D. Pp. 77. Cleveland, Ohio: Published posthumously for Private Distribution by the Cleveland Medical Library Association.

THIS book by the late Dr. Handerson, is of interest to the antiquarian as a picture of medieval medicine, containing as it does a fascinating description of intestinal surgery, with an account of the use of drainage tubes of alder. The work reflects much credit upon the author's industry in a research, which now the public is permitted to enjoy. E. H. G.

WAR SURGERY FROM FIRING LINE TO BASE. By BASIL HUGHES, Temporary Major, R.A.M.C., T.F., and H. STANLEY BANKS, Captain, R.A.M.C., T.C. with special chapters by Lieut.-Colonel L. F. Smith, R.A.M.C., and Miss C. Bilton, R.R.C., Q.A.I.M.N.S., and an introduction by Col. Sir T. CRISP ENGLISH, Consulting Surgeon to the British Forces in Italy. Pp. 623; 373 illustrations. New York: William Wood & Company, 1919.

OF the many books that have recently appeared on military medicine and allied topics, this volume seems to take the honors, because of the interesting manner in which the subject is presented. Although by title it is a treatise on war surgery, in fact it represents the personal experiences of two British medical officers who had spent three and one-half years both in the Western and Eastern theaters of war. During this time they were attached to regiments on the firing line for eighteen months, with a field hospital eight

months; they were with a busy casualty clearing station in France for four months and spent a year at a base hospital in the East. All of their statements are based upon personal observation, and most of the subjects are illustrated by actual case histories. The reader's interest is held throughout by the entertaining narrative style, including the use of many words of trench slang, which gives a wonderful insight into the life and hardships of the soldier as well as the surgery of the war.

Bacteriology and wound infections, as may be expected, have been extensively considered; in fact, many of the details of laboratory technic could have been omitted without detriment to the general value of the book. The chapters on war wounds are fascinatingly gruesome, and it is of interest to note that the Carrel-Dakin technic, when properly and systematically applied, has been found to be far superior to the other treatments. In addition to the discussion of the purely surgical aspect of the soldier, the book contains many valuable pages on trench diseases and trench life, not to mention the discussion of the effects of tropical diseases on war wounds and the special effect of aviation on otherwise simple wounds. F. B. B.

THE ACTION OF MUSCLES, INCLUDING MUSCLE REST AND MUSCLE REËDUCATION. By WILLIAM COLIN MACKENZIE, of the Staff of the Military Orthopedic Hospital, Shepherd's Bush, London. Pp. 267; 99 illustrations. New York: Paul B. Hoeber.

THIS is a book of interest alike to orthopedists, neurologists and anatomists. In it the muscles are treated from the viewpoints of physiological action, comparative anatomy and loss of function after nerve injury. All these are used in leading up to the consideration of physiological rest of muscles and reëducation. As the muscles constitute 45 per cent. of the total weight of the body, one can readily agree with the author that they are entitled to more scientific consideration than they usually receive. Since the muscles are dependent upon the nerves for their proper functioning, they may be regarded as the end-organs of nerves. In muscle paralysis after nerve injury the greatest care and attention is paid to the nerve, but usually the muscles are quite neglected. It is the author's purpose to try to bring out more prominently the needs of the muscles after nerve injury. To do this he first thoroughly examines into the action of certain muscles, or groups of muscles, having the same innervation. He does not try to cover all the muscles of the body, but selects those of greatest practical importance. Thus, under ulnar paralysis, he carefully goes into the function of the muscles innervated by the ulnar nerve. In this consideration of the

action of muscles he is quite complete and understandable, which is a contrast to some of the anatomies, where the action of muscles is stated often in a single sentence. From this careful analysis of the action of the various muscles involved he deduces the position of physiological rest for the arm and hand in ulnar nerve injury. Then, with the aid of photographs of patients, he explains his method of reëducation of these muscles, showing the sequence of joints to be exercised and the method of procedure. After the operation of suture for complete division of nerves the author considers that these movements should be tested for and encouraged, as soon as the surgical state of the wound is considered satisfactory. In a similar way he takes up the other important groups of muscles, and in each brings out many valuable points in treatment, based on the careful analysis of their normal physiology. W. H. F. A.

THE ORGANS OF INTERNAL SECRETION. By IVO GEIKIE COBB, M.D., M.R.C.S. Pp. 274. New York: William Wood & Co., 1919.

As shifting as the eternal sands, goes on the shifting of our knowledge of endocrinology. Were each gland which has an internal secretion as its principal possession, to exhibit its structural pathology and its pathological physiology, in a manner independent of its fellows, how easy the subject would be! It is true that certain glands do exhibit certain clinical signs which focus the attention upon them, but with our ever broadening knowledge of endocrinology and hormonology what must one conjecture of the effect of this morbid change on other glands?

It is in a stage which, for want of a better term, we must name the "conjectural" that we seem to be anno domini MDCCCCXIX, and it is for this reason that the book under consideration leaves us unconvinced; not from the lack of ability of the author, but from the lack of evidence which writers on endocrinology have presented. Some of the cases, which Cobb describes, he has benefited by organ therapy without telling us on what deduction he based his treatment. Mixtures of extracts of many glands, well named according to modern ordnance terms, "mitrailleuse," by Leonard Williams, are used, but we search in vain for the reason and question, unanswered, "why"?

We commend the book, however, to those who wish to be brought up to date with endocrinology, for the literature has been well studied, sifted and assorted and we have as a result, a good compilation, containing perhaps, to those of venturesome disposition, many important suggestions. E. H. G.

AN INTRODUCTION TO THE MAMMALIAN DENTITION. By T. WINGATE TODD, Professor of Anatomy in the Western Reserve University, Cleveland, Ohio. Pp. 290; 100 illustrations. St. Louis: C. V. Mosby Company.

THIS is an interesting book on Mammalian teeth and skulls. If, as the preface seems to indicate, the author intends it for the dental undergraduate, he surely has a high opinion of the mental capacity of that individual. It would seem to be more adapted to an advanced college course in comparative anatomy, where specimens could be examined in detail by each member of the class. The author aims to follow out the evolution of tooth-forms from early mammalian and reptilian ancestors and to show how the various modern mammalian dentitions have been arrived at. In doing this he presents the American views regarding the evolution of tooth-forms and adopts the tritubercular theory of Cope and Osborn, in its most recent form, as his basis. In taking up the various mammalian orders in detail, he emphasizes the relationship between life habits and dentition. The illustrations are from photographs of actual jaws and skulls, and these, while giving the general aspect very well, sometimes fail to bring out the details necessary for a clear understanding of the text. These details might well have been shown by the insertion of little diagrams of the teeth at the side of the photographs. W. H. F. A.

ANNUAL REPORT OF THE DEPARTMENT OF PATHOLOGY OF THE JOHNS HOPKINS UNIVERSITY AND HOSPITAL. Fasciculus No. 2 of Vol. XVIII of the Johns Hopkins Reports, 1917. Pp. 342, with numerous figures. Baltimore: Johns Hopkins Press.

WE have here published under one cover accounts of the work conducted in the pathological department of the Johns Hopkins Medical School during 1917; all communications hitherto unpublished are presented in detail, as likewise articles which have appeared in various journals. Twenty-four papers are included, in addition to autopsy statistics and various reports; numerous excellent illustrations are given. A wide range of subjects are dealt with, including studies in gross pathology, pathological histology, immunity and metabolism, indicating the broad interests of this department. The individual papers are generally excellent and in accord with the well-established reputation of this department for thorough work and splendid reports. J. A. K.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL, ST. AGNES AND NORTHEASTERN HOSPITALS.

Gunshot Affections of Large Joints.—Daw (*British Jour. of Surg.*, October, 1918, vi, 191) says that gunshot injuries generally lead to very severe forms of obstruction to the normal movements of joints. Manipulation has its chief use in the correction of deformities, and in changing the position of a joint from one in which function is bad to one in which function is at its best if permanent stiffness is to be the final result. Improvement of mobility is more likely to be gained by slight movements followed by periods of rest or by slow stretching of contracted parts—in other words, by gradual change of position—rather than by forcible movements through a large range. Open operations to obtain mobility are rarely advantageous except in the case of the elbow-joint, where they are usually satisfactory. Massage and baths are valuable adjuvants to improve circulation and aid in the dispersal of scar tissue. Passive movements have a very limited value, and are often harmful. Active movements, especially those of normal use and occupation, are most valuable, and will often do more to increase mobility than any surgical means at our disposal.

Treatment of Ununited Gunshot Fractures.—Groves (*British Jour. of Surg.*, October, 1918, vi, 203) says that the introduction of a living autogenous bone graft is the main resource for the treatment of ununited fractures, and especially for those in which there has been a definite loss of substance. The existence of latent sepsis and the presence of extensive scars of skin, muscle and bone, however, make it much more difficult of success than when it is applied for the replacement of bone lost by disease, *e. g.*, a tumor or tuberculosis. The essential condition to be obtained in the graft bed is the removal of scar tissue, whether cutaneous, fibrous or osseous. Ragged bone end must be removed and no dependence placed upon them for osteogenesis or union. That a living autogenous graft continues to live when joined to living bone is

no longer a matter of theory or microscopic investigation. When it becomes fractured it produces callus just as does a living bone. That periosteum is not an essential element in the graft is proved by the fact that in many cases a naked bone graft heals in position and becomes united to its bed. The best example of this is in the living tibial peg driven into the neck of a fractured femur. Nevertheless the preservation of the periosteum is very desirable in all cases except those where the graft is entirely intramedullary. The role of the periosteum is remarkably demonstrated by the comparison of three types of operation: (1) Where the naked graft is used, increase in thickness of the graft, even after long survival, is very slow. Whenever sepsis supervenes, the graft becomes entirely exfoliated without depositing any new bone. (2) Where periosteal flaps with a thin layer of bone are turned down to bridge the gap, no new bone is deposited, and failure results. This shows that periosteum, even when retaining its attachment, will not deposit new bone in an adult. (3) Where a graft covered on one surface by its own periosteum is used, its behavior is different from either of the above groups. Increase in thickness occurs in all cases within a few months. In those cases in which secondary sepsis supervenes, there is an abundant deposit of new bone between the periosteum and the graft. The solid portion of the graft may be exfoliated, but a mass of new bone is left behind of larger bulk than that originally used. From these facts it may be inferred that the osteoblasts necessary for new bone formation are contained in the dense bone, but that the protecting and vascularizing matrix of the periosteum is necessary for their activity. The success of all plastic surgery depends largely upon accurate suturing. Bone being a tissue of slow growth and slow repair, requires more firm and lasting sutures than the soft tissues. There are three methods used for the fixation of a graft: (1) Suture by ordinary absorbable sutures; (2) fitting by accurate joinery; (3) fixation by means of metal screws, pins, wires, or plates. The series reported by Groves, contains 34 cases of autogenous bone grafting. Of these, 10 (29.4 per cent.) have been failures, 5 (14.7 per cent.) have been eventual successes in producing bone union after extrusion of the graft, and 19 (55.8 per cent.) have been complete sucesses.

Changes in Growing Bone after Injury to Epiphyseal Cartilage Plate.—Haas (*Jour. Orthop. Surg.*, 1919, i, 67) says that the longitudinal growth of bone is maintained by changes taking place in the epiphyseal cartilage plate. As long as this highly differentiated cartilage mass persists there is opportunity for further increase in length, but with its ossification there is loss of that property. As a working principle it is necessary to know the exact portion of the epiphyseal cartilage plate that is most essential to bone growth. The greatest growth activity is localized in the cartilage columns of the epiphyseal cartilage plate and after the destruction of this portion of the plate, length growth practically terminates. The metaphyseal cartilage serves chiefly as a medium for or is the site where the newly formed cartilage is transformed into osseous tissue. For the proper functioning of the epiphyseal cartilage plate it is essential that it shall receive an adequate blood supply. If all the bloodvessels entering the bone in this region of the plate are destroyed, a very marked loss of growth takes place. This

loss of growth is much greater than when the nutrient artery is destroyed. Closely associated with the bloodvessels is the character of the constituents of the blood. If there is lacking some necessary chemical elements a loss of growth is likely to take place. Thus in certain diseases and in abnormalities of the endocrine system disturbances in growth frequently occur. Trauma is the most frequent cause of disturbances in growth of bones. It must be remembered that an injury in the region of the epiphyseal cartilage plate may be confined entirely to the superficial tissues, to the deeper tissues containing the vascular supply to the epiphyseal cartilage plate, to the epiphyseal cartilage plate itself or may be a combined injury of more than one of these structures. Upon the severity of the destructive process to these vital growing parts depends the resulting disturbances in growth.

Study of Buried Bone.—Cowan and Ely (*Jour. Orthop. Surg.*, 1919, i, 101) made their study upon a series of knee-joint resections in the dog. A patella or the fragment of another bone, embedded fresh in the muscles of the animal from which it was removed, has a tendency to disappear, but does not disappear at least for a long time. In none of their cases had it disappeared completely. Its structure becomes less dense. The bone tissue itself may be replaced by fibrous tissue, especially at or near the circumference, or it may be absorbed. Absorption is the rule in the interior. Occasionally typical rarefying osteitis by osteoclasts is seen. More frequently the process seems to be one of simple absorption—"halisteresis." The method of absorption is often difficult to determine, for about many of the trabeculæ there are no giant cells, no leukocytic infiltration, and no increased vascularity of the marrow. Many of the cells disappear early from the bone. Others stain well after the expiration of a long time. Death of bone is the rule. A patella, with a complete investment of bone and cartilage, does not resist absorption better than a bone fragment whose marrow is exposed to the surrounding tissue. A blood supply is established in the marrow of the buried bone. The marrow has a tendency to become fatty and fibrous, though lymphoid paths may persist. It is engorged in animals who have died with an acute infectious disease, as is the marrow of normal bone in such circumstances. In other words, it is functionating as marrow. Cartilage becomes eroded at its surface, and is replaced by fibrous tissue. Sometimes it disappears completely in areas. Its cells often stain well after a long time. Sometimes they die after a shorter time. The buttress underneath the cartilage almost always disappears early. Roughly, the changes in bone and cartilage are the same as those seen in atrophic, or proliferating arthritis.

Abduction Treatment of Fracture of the Neck of the Femur.—Whitman (*Surg., Gynec. and Obst.*, 1918, xxvii, 578) says that nonunion occurs in childhood under the same circumstances as in adult life, although there can be no question of the capacity of the tissues for repair. Repair after non-union is the rule when at open operation the fragments are freshened and adjusted, indicating that fixation in apposition is the first essential of success. Experience in bone grafting proves that union is possible under far less favorable conditions, as regards the blood supply, than in fracture of the neck of the femur. The obstacles

to repair, whether intrinsic or extrinsic, actual or fanciful, that have thus far justified inadequacy and neglect furnish the strongest presumptive evidence in favor of opportunity as the determining factor in the result. It has been already abundantly proved by practical experience that repair is possible in every variety of fracture at the hip and at any age, and although it cannot be asserted that opportunity will always assure success, it is self-evident that want of opportunity assures failure. Consequently, the responsibility for opportunity, upon which the result is primarily dependent, rests upon the one who selects and applies the treatment. This conclusion, however revolutionary as contrasted with conventional teaching, is, in effect, simply that surgical principles, whose application has been made practicable by the abduction method, should now govern the treatment of this as of other fractures.

Shall Operation for Hypertrophied Prostate be Done in Two Stages.—WRIGHT (*Surg., Gynec. and Obst.*, 1919, xxviii, 56) says that all cases, including those where only a small amount of residual urine is present, should be given several days of preliminary drainage before prostatectomy is done. Since cystotomy, which gives permanent drainage to the bladder and the pelvis of the kidneys, has been followed by death, the author believes it is better that drainage should be made by use of the catheter. Cystotomy should be reserved for use in those cases where catheterization, for any reason, is impossible; or, for use in those cases of acute cystitis that do not do well with permanent catheter. Since uremia has been known to follow the opening of a bladder which contained only 45 c.c. of residual urine, if compelled to do a cystotomy, it should only be performed after catheterization or aspiration of the bladder has been carried on for several days.

Carcinoma of the Stomach.—DOUGLAS (*Surg., Gynec. and Obst.*, 1919, xxviii, 76) says that the conclusion reached by the pathologists of the Mayo Clinic where probably more material from excisions of ulcers and early carcinomata are examined with the greatest care than anywhere else in the world, should carry great conviction, even considering the work of Bullock. The considerable but not tabulated reports in cancer in a small area of the edge of an old ulcer, is proof positive that the change does occur, confirming the above statement. The evidence that cancer develops from chronic irritation and ulcers in other localities, adds probability that the same metamorphosis occurs in the stomach. The agreement of those who are opposed to the theory of carcinomatous degeneration in a large percentage of ulcers that a previous ulcer history may be obtained in from 5 to 17 per cent. together with the facts that diagnosis is not always certain, and that ulcers may perforate without previous symptoms, and that a long ulcer history is not contrary proof, would seem at least to make it a fair presumption that ulcer preceded cancer in a larger percentage of cases than their figures indicated. The results after gastro-enterostomy are the strongest presumptive evidence against carcinomatous degeneration of ulcers, but an explanation is not inconceivable, based on the rapid healing which usually occurs in ulcers near the pylorus after operation, and the theory of a possible inhibition of cancer formation after gastro-enterostomy, according to the theory of Gressot, on the possible digestion of

sloughing carcinoma, and remembering the claim that a large percentage of cancers originate in ulcers does not mean that a large percentage of ulcers necessarily become malignant. The following facts are not contested: (1) The mortality without operation is 100 per cent.; (2) the percentage of deaths from cancers of the stomach in the total death-rate is 1 per cent. (3) More than 30 per cent. of all cancers occur in the stomach. (4) Of late years the statistics at the large clinics show an operability of 38 (Mayo) to 39 (Bloodgood) per cent. of cases coming to the surgeon. Gastric ulcers are potentially cancer and a diagnosis macroscopically in the early stage of malignant development cannot be made; therefore, an old callous ulcer in a patient of the cancer age should, when possible, be excised. If small and not believed to be malignant, and only then, it may be destroyed by the cautery method, and a gastro-enterostomy done, or else a transgastric resection or pylorectomy performed whenever it seems even possible that carcinoma has begun at any point in the margin of the ulcer.

THERAPEUTICS

UNDER THE CHARGE OF

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Treatment of Influenza.—From October 10 to December 9, 1918, there were admitted to a general hospital, B. E. F., France, 937 cases of influenza. Nearly all showed pulmonary symptoms and were serious in about one out of every four. The mortality was 2.77 per cent. SMALL and BLANCHARD (*British Med. Jour.*, March 1, 1919, 241) believe that this compares favorably with the death-rate in other places and therefore outline the treatment employed. The general management was that of a fever. As far as possible the patients were treated in the open air, a sufficiency of blankets, etc., being employed to ensure warmth. The diet consisted mainly of fluids—milk, beef tea, egg flips, etc.; beef tea they consider especially valuable because of its stimulating properties. The drinking of large quantities of fluid was encouraged for the promotion of elimination and the lessening of toxemia. The degree of debility produced was often extreme and was particularly associated with circulatory symptoms as well as marked general weakness. Absolute rest during the acute stage is of paramount importance. In the severer cases alarming symptoms followed any degree of movement. Sleep they consider of the utmost importance. The patients were given heroin, gr. $\frac{1}{12}$ hypodermically, repeated once or twice, if tepid sponging proved insufficient to induce sleep. The patients were arranged in groups (unselected) of 15 and were put upon different drugs and the progress of the various groups noted and compared. Aconite, aspirin, sodium salicylate, belladonna, arsenic,

quinin, Dover's powder and gelsemium were tested in this way. None of them appeared to have the slightest influence, except belladonna (which showed evidence of beneficial action in a number of cases) and gelsemium. The patients treated by this drug improved in a manner far exceeding those given any other treatment. After a few doses they felt much better in every way. In most the temperature speedily commenced to fall and the improvement in the general condition was obvious. So great was the contrast that it was usually possible, without previous knowledge, to pick out the cases treated with this remedy. Beyond slight ocular disturbances in a very small number of cases they did not see any disadvantage in its use. When stimulants were indicated, alcohol (brandy, whisky or champagne) gave the best results, half an ounce every four hours or oftener if the case was urgent. Caffein, strychnin, adrenalin and pituitrin produced no beneficial results.

Fatigue in Irritable Heart and Other Conditions.—Following Ryan's observation that general fatigue causes measurable shortening of the time interval between the appearance and fading of the white vasomotor reflex which is produced by stroking the skin with a blunt-edged instrument, KING (*Arch. Int. Med.*, 1919, xxiii, 527) made several hundred tests on soldiers suffering from "irritable heart" and other conditions. The "irritable heart" group are classified as physically inferior, constitutionally inferior, emotionally sensitive and neurotic, after Campbell; the smaller, organic group represents all patients with demonstrable cardiac lesions; a third group (post-infection) contains those patients developing symptoms of irritable heart after an acute infection, but in whom no organic disease of the heart can be demonstrated. After a review of the literature and a consideration of the nature of the phenomenon, King gives the following conclusions: (1) The quantitative estimation of fatigue by the white vasomotor reaction, as suggested by Ryan, is of value in the study of clinical conditions. Owing to the various sources of possible error in the test, it is more suitable for group study than for individual cases. (2) The day curve of fatigue estimations is much the same in the several groups of cases that have the syndrome of irritable heart as in those with organic heart disease. (3) Patients with irritable heart who fall into the groups of general constitutional inferiority or pure physical inferiority show very rapid fatigue on exercise. This fatigue can be measured and is an actual physical phenomenon and not of psychic origin. (4) There is a correspondence between the general body strength and the duration of the white vasomotor reflex. This suggests that there is a relationship between the strength of the skeletal musculature and the arteriolar musculature in a given individual. It is not considered, however, that the test is accurate enough to warrant estimating body strength from the vasomotor reflex in an individual case. (5) An unusual type of day fatigue curve, of V-shape, is usually found in patients convalescent from influenza. It is unlike the day curve obtained in any ambulant patient and may be characteristic of convalescence.

OBSTETRICS

UNDER THE CHARGE OF

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Influenza Occurring in Pregnant Women.—HARRIS (*Jour. Am. Med. Assn.*, April 5, 1919) has collected the statistics from 1350 cases of influenza complicating pregnancy. His results are tabulated and the conclusions are drawn from the examination of the tables. About half the pregnant women having eclampsia developed pneumonia, and of these 50 per cent. died, a gross mortality of 27 per cent. In those developing pneumonia the mortality was higher in the last three months of pregnancy. The largest number of cases occurred in the sixth, seventh and eighth months of gestation and the smallest number from the third to the fifth month. As regards the first two months of pregnancy, in many instances undoubtedly the existence of pregnancy was not suspected by the attending physician, and therefore these cases are not included in the reports. It seems too far to conclude that the pregnant woman is not more susceptible to the disease in any one month of pregnancy than in another. The disease was distinctly most fatal in the last three months of gestation. Sixty per cent. of the cases developing pneumonia in these months proved fatal. The mortality curve reached its highest point in the ninth month, with 61 per cent. When the gross mortality is reckoned the percentage is reduced somewhat, owing to the large number of cases reported for this period. In 626 cases uncomplicated by pneumonia, pregnancy was noted in 26 per cent., the ratio being somewhat higher in the first three months. This is not much in excess of the frequency of abortion one would expect under ordinary conditions. It must also be remembered that many of these abortions might have occurred in the absence of influenza or that this disease may have served only as a terminal factor in causing the expulsion of the ovum already abnormal. In cases complicated by pneumonia the interruption of pregnancy occurred in double frequency, being 52 per cent. in 585 cases. The first two months of pregnancy are disregarded, the percentage of pneumonia is still higher, the termination of pregnancy occurring in 62 per cent. of 308 cases. It is commonly believed that influenzal pneumonia almost always causes the interruption of gestation, but the surprising fact is that in 38 per cent. of the fatal cases the patients die without the interruption of pregnancy. This would indicate that when the ovum is normal and the placenta normally situated and developed the patient may pass through an extremely severe disturbance without causing the termination of pregnancy. In 743 patients in whom pregnancy was not interrupted mortality was 16 per cent. In 468 cases in which pregnancy was terminated mortality was 41 per cent. This ratio remains throughout the different stages of pregnancy during the first two months, but it has already been pointed out that regarding these two months it is difficult to draw definite conclusions. Unquestionably the interruption of pregnancy at any time makes the

prognosis more grave. In cases complicated by pneumonia in 383 patients where pregnancy was not interrupted the mortality was 41 per cent. But the mortality was 63 per cent. in 395 patients where pregnancy terminated. It is possible from this data to construct an algebraic formula by which the mathematical probability of an interruption of pregnancy can be calculated. It may be concluded that the chances of the interruption of pregnancy are about doubled if the woman contracts both influenza and pneumonia over what they are if she has only influenza. Obstetricians usually believe that normally and without known complications abortion occurs once in five pregnancies. This ratio does not seem to be much altered by the presence of influenza alone. The mortality of influenza complicated by pneumonia in pregnant women is greatly increased by the interruption of pregnancy. The conclusions drawn from the study of these cases are that pneumonia complicated influenza in pregnant women in about half the cases. Of these patients 50 per cent. died. The mortality was greatest during the last three months. The gross mortality of all cases was 27 per cent. In cases without complication, pregnancy was interrupted in 26 per cent., and in those where influenza was complicated by pneumonia in 52 per cent. In the fatal cases of whatever sort, abortion or premature labor occurred in 62 per cent. Thus in 38 per cent. of the fatal cases the patient died without the interruption of pregnancy. When pregnant women suffered from influenza and had abortion or premature labor their mortality was 41 per cent., and when they escaped the interruption of pregnancy the mortality was 16 per cent.

Influenza in the Newly Born Infant.—ABT (*Jour. Am. Med. Assn.*, April 5, 1919) reports the case of a primipara who developed influenza. Labor developed in twenty-four hours after she was taken ill with influenza. The fetal heart sounds became rapid, but remained regular and indicated no disturbance of the fetal circulation during labor. When the amniotic liquid was discharged it was markedly stained with meconium. The child, a male, weighing six pounds twelve ounces, was spontaneously delivered. The infant's skin immediately after labor became grayish blue, and although the child cried strongly and the air passages seemed to clear this condition persisted. The child breathed promptly after birth and it seemed vigorous. Ten minutes after birth fine moist rales were heard in both lungs, but there was no dulness on percussion. On the following day the child was put to the breast and nursed well, but shortly afterward the breathing became rapid and labored. The respiration rose to 120. The temperature never exceeded 100°, falling to 97°. Cyanosis increased; respiration was superficial and rapid and the child occasionally uttered a weak cry. Examination of the baby's blood made on the day before its death showed a leukocytosis of 21,450, with a few of the nucleated red and some large pale white cells not classified. The polymorphonuclears were 58 per cent., the lymphocytes 35, large mononuclears 2.8 per cent., and eosinophiles none. During the third day of the infant's life finely crepitant rales appeared, particularly diffuse over both lungs. Cyanosis and dyspnea appeared and death occurred. At autopsy there were minute hemorrhages in the pericardium. The heart muscle was flabby, giving evidence of a parenchymatous myocarditis. On the heart valves there

was evidence of a beginning acute endocarditis involving especially the tricuspid valve. In both lungs there was confluent hemorrhagic bronchopneumonia. The spleen showed inflammation, with edema and passive hyperemia. In the kidneys there was no gross pathological change, and in the liver there was cloudy swelling. Cultures made from the organs of the child showed abundant colonies of streptococci. Over the lungs there were also a few colonies of Staphylococcus aureus and albus and many colonies of streptococci. Examination of the organs showed diffuse bronchopneumonia, streptococcus, septic nephritis, acute infection of the spleen, the streptococcus being the cause of the condition. The mother of the infant had a mild attack of influenza and recovered without complications. We must believe that the child was infected before birth.

Placental Tissue as a Galactagogue.—CORNELL (*Surg., Gynec. and Obst.*, November, 1918) had the placenta of cows prepared by washing and drying and putting up in 5-grain capsules. These were given four times daily for twelve doses. The first dose was given as soon as the patient was able to take nourishment and had rest after labor. This generally occurred within twelve hours after delivery. There was no disturbance in digestion, and while a few patients objected to the odor of the preparation, aside from this there was no trouble. The placenta was used in more than 100 cases, but as the results were not satisfactory in the first cases only the last 100 cases have been selected. To compare methods of treatment, 70 other patients in the hospital at the same time and on the same floor and using the same food were investigated to observe their lactation. In the small ward containing three beds one or two of these patients would receive placental tissue while the other would not, but the patients were cared for by the same nurses. The results are tabulated, showing the age, nationality and general health of the patient, the method of delivery and the character of the puerperal period. It is concluded from this study that placental tissue has a favorable effect in the production of breast milk. The nationality, age and general condition of the mother and the sex of the infant have no influence on this result. Of those mothers who did not receive this preparation their infants began to gain on the fourth and fifth day after labor in 69 per cent. of the cases. Of those mothers who received this preparation their infants began to gain in weight on the fourth and fifth days after labor in 87 per cent. Of those mothers who did not take the placental extract, 24 per cent. of their children had regained their birth-rate before leaving the hospital, while of those who had taken the placental extract 44 per cent. regained their weight. The reviewer has recently tested dried placental extract in 3-grain doses, given three times daily after food, for several weeks. The results have been distinctly favorable, especially in women whose general nutrition was poor and when the general development of the woman was considerably below par.

Rotation of the Head by Forceps in Occipitoposterior Position.—BILL (*Am. Jour. Obst.*, December, 1918) has rotated the head with forceps in 249 cases. In 170 the position was right occipitoposterior and in 79 left occipitoposterior. In 104 cases the head was at the pelvic brim,

its greatest diameter not having passed through. In 88 cases the head was in the pelvic cavity above the spines of the ischia and had not entirely passed through the os. In 43 the head was in the pelvic cavity and had entirely passed through the os and in 14 the head was at the pelvic outlet. Among these 14 cases were 11 in which the occiput had turned into the hull of the sacrum, the sagittal suture lying in the antero-posterior pelvic diameter. The forceps was applied to the sides of the head and the head rotated through the smaller arc of the circle. This varied from 100 to 180 degrees. There was no difficulty in any of these cases and the first essential was the accurate diagnosis of the exact position of the head so that the forceps could grasp it with an accurate application. If the instruments are turned in such a manner that the blades lie continually in the same axis any sort of good forceps may be used. Those with solid blades are preferable because they are more easily applied, the blades take up less room in the pelvis, the smoothness of the blades helps the rotation and they are more easily removed after the rotation is complete. The concavity of the pelvic curve with forceps should look toward the front, that is toward the child's face, in cases of posterior position. So far as the child's head is concerned this in reality gives a reverse application of the forceps. Complete flexion must be secured before the forceps blades are locked. The handles are then raised in the direction of the child's face and then carried around in a large circle, first toward the patient's thigh and then posteriorly. This tends to favor flexion of the head and a large sweeping movement of the handles tends to keep the blades of the forceps in the same axis throughout the rotation, thus allowing the head to turn without difficulty. Traction is not made until the head is in the normal anterior position, and if the rotation be properly carried out no force is required during the rotation. The handles of the forceps must not be twisted but must be carried through a large circle and traction must never be made while rotation is being accomplished. If the head is too firmly fixed in the pelvis its position may be altered slightly in order to effect rotation. The head should never be drawn down first before rotation is performed. After rotation is complete the forceps occupies a reverse position and the instrument must be removed and reapplied; but before removal it is well to make slight traction and fix the head in its new position and prevent a return to the old position. In very rare cases the head slips back before the reapplication is made and has outturned again. In making the reapplication the posterior blade should be first inserted and applied. After rotation there is usually very little difficulty in effecting delivery. While manual rotation has in some cases proved satisfactory, the forceps is better, as it gives more efficient control of the head. The operator must decide in each case as to the best time for carrying out each maneuver. The essentials of success in this method of treatment are the absolute diagnosis of the position and true cephalic application of the forceps, rotation without traction. The sweep of the handles of the forceps through the large circle, very slight traction to fix the head in its new position and the application of the posterior blade first and the second application of the forceps. This maneuver eliminates the necessity for excessive force in the delivery of abnormal cases and makes comparatively simple and easy the extraction of the head when it presents with the posterior position.

GYNECOLOGY

UNDER THE CHARGE OF

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Cure of Prolapse in the Aged. — The gynecologist is frequently troubled to know how to treat effectively the very old women who suffer from complete prolapsus of the vagina and uterus, especially when the vagina hangs down between the thighs, becoming thickened and often ulcerated. These patients are usually too old to stand a long operation and only an extensive operation will be effective since all the attachments of the uterus and vagina have been destroyed and the atrophic muscles of the perineum are so feeble that they give little chance of a perineal repair. In such cases McArthur (*Med. Jour. Australia*, 1919, i, 149) suggests an operation that resembles a coat sleeve that has been sewed down the center and which therefore cannot be inverted. The operation is performed by stripping an area of mucous membrane from the anterior vaginal wall, about a finger breadth in width from just behind the orifice of the urethra to within 1 or 2 cm. of the junction of the cervix and vagina. A similar area is stripped from the posterior vaginal wall and then sewn together with a continuous catgut suture the anterior and posterior cut edges on the left side, followed by a similar suture on the right side, sewing three or four sutures on the left side, then a few sutures on the right side and thus alternating until both suture lines are complete. As the stitches are pulled taut, the cervix recedes into the vaginal orifice until it is lost to touch. The next procedure is to complete the perineorrhaphy by inserting three or four sutures into the already denuded perineum, tying them and completing the closure of the cut edges of the vaginal mucous membrane. When the operation is completed, there is practically a double vagina which prevents prolapse but at the same time allows the discharge of uterine secretions. The operation can be done very quickly and thus is especially serviceable in debilitated aged women.

Radium in Cancer.—Skepticism in regard to the value of radium in the treatment of malignancy is rapidly disappearing on account of its extensive use and the brilliant results that have been achieved in many cases especially in epithelioma, fibroids and as a palliative measure in inoperable cancer. It is now generally agreed by the surgeons of the largest clinics that radium is a valuable adjunct in the treatment of malignancy. In some places it is used only as a palliative procedure while in other places it is also being used as an anti-operative treatment. In discussing this matter Boggs (*New York Med. Jour.*, 1919, cix, 488) reminds us that several factors have brought radium into disrepute and have given the impression that the claims made were unjustified. Chief among these is allowing patients and the physicians who refer them to us to expect a permanent cure when only palliation and prolongation of

life is all that any one with ordinary medical intelligence could expect. The patient often cannot receive much palliation from any other method of treatment, but by the use of radium will improve rapidly for a time, or even a clinical cure will be obtained. Finally, on account of the extensive metastases, the patient will die after from six months to three years or more of prolongation of life. Then those who were watching the case or those who knew that radium had been used, will decide that radium had no value, without remembering or knowing the condition of the patient when radium was started. If one is to express an opinion as to the therapeutic value of a remedy, such statements should be guarded unless a study of all factors has been made and one should be without prejudice for or against the remedy. Many operators have used insufficient quantities of radium thus giving inefficient doses, or else, on the other hand, have overtreated the local growth, without attempting to treat the metastases. No one will deny that, under certain circumstances radium may be harmful rather than beneficial, since if the dose is too small or too long continued, stimulation rather than destruction may take place while, on the other hand, too large a dose may result in irreparable damage to normal tissues. Treatment of hopeless carcinoma in the past has been with morphin, but today, the author believes that it should be by radiotherapy since it is pitiful that patients with inoperable cancer, after their condition is pronounced hopeless, receive so little consideration. However, he cautions that thorough knowledge of the action of radium is essential because from that knowledge only may the proper dose be applied to produce the best results and haphazard use of radium should be discouraged. In estimating the value of radium therapy, its advocates do not claim that it supersedes surgery, but that it is a valuable adjunct to surgery, in helping to prevent recurrences after operation and in rendering inoperable cases operable and that it has proved itself one of the best palliatives we have in cases in which operation is impracticable and in many of such cases has brought about an apparent cure. In recurrent and inoperable carcinoma of the uterus, Boggs believes that radium might be considered the specific treatment, because it is the only method which retards the process to the same extent and gives the same amount of palliation. Radium is always less valuable in recurrent than in inoperable carcinoma of the uterus and since so much has been accomplished in the inoperable cases, in every primary case, no matter how early the operation has been performed, Boggs believes that there should be either ante- or postoperative treatment with radium, or both.

Operative Results in Myoma Uteri.—There were 262 cases operated upon for uterine myomata at the Woman's Hospital in New York City during the year 1918, with a mortality of 4 patients, or 1.52 per cent., according to a report which has been published by BROUN (*Am. Jour. Obst.*, 1919, lxxix, 333), and 2 of these patients died of embolus. The remaining deaths were caused in one instance by intestinal obstruction occurring eight days after myomectomy associated with a ventral suspension and removal of tuberculous appendages, while the other death followed within three days after a supravaginal hysterectomy and removal of purulent appendages. The 2 deaths from embolus in

the present series of 260 cases taken in connection with 7 from a similar cause in the 1500 cases operated on during the eight years previous, in which there were 28 deaths from all causes, gives embolus as the largest causative factor in the fatal terminations. The next highest cause was peritonitis in 7 of the fatal cases. In accordance with the usual routine of the day, a follow-up investigation was conducted upon these patients, of whom, 117 patients reported for examination. Of this number, 99 were in excellent condition from a surgical standpoint, and stated that they felt absolutely well; 5 patients complained of menopausal symptoms, and their ages ranged from thirty-three to forty-two. In 3, both ovaries and tubes had been removed, and in the remaining 2, one ovary and tube had been saved. The few patients complaining of the forced menopause is striking, especially when one considers the 113 patients examined in whom there is no record of any symptoms except of a passing character which caused no inconvenience. It may be argued that these patients are hard-working women and not given to noting symptoms, which would be distressing to those of the more-leisure class, which no doubt, is true to a great extent. Nevertheless, Broun strongly believes that in the presence of tumor growth the function of the ovaries from the standpoint of internal secretions is greatly diminished and in this class of cases their importance in maintaining the nervous equilibrium of the patient is to a great extent overestimated. At any rate, this belief is apparently borne out by the study of these cases under consideration where usually one or both adnexa have been removed on account of circulatory changes or infection. Unless there is some special reason, such as a possible pregnancy, why should an ovary be conserved after its tube has been removed? The author thinks it better surgery to remove the ovary at the time the tube is excised and certainly in instances of the removal of the uterus and the remaining adnexa. This opinion founded on clinical experience is borne out by Sampson's studies of the tubal and ovarian circulation, since he has shown by his combined tubal and ovarian vascular injection specimens, that much care must be exercised in removal of the tube in order not to disturb the ovarian circulation and at times this disturbance is impossible to avoid on account of the abnormal distribution of the vessels. The results here reported by Broun represent the end-result of surgery applied to a series of consecutive cases by the full operating staff of the hospital and he doubts whether they can be equalled by roentgen rays or radium even in selected cases, especially when we consider the contraindicating, unrecognizable degenerative changes present in such tumors and also the associated pathological conditions in the adnexa. Therefore, he would use radium or the roentgen rays in myomata for the purpose only of controlling bleeding and then only when the contents of the pelvis can be clearly mapped out. They are a valuable means under such conditions and by their use, what would otherwise be a mutilating operation, can be avoided.

Lacerations of the Vagina from Coitus.—Coitus as the cause of a laceration of the vagina except in cases of rape or marked disproportion between the penis and vagina is quite rare and consequently it is interesting to note that one case of this kind has been reported by STOKES

(*Med. Jour. Australia*, 1919, i, 111) and two other cases have been reported by D'ARCY (*Med. Jour. Australia*, 1919, i, 172). All three of these patients had had children although in one of the cases, the ovaries had been removed several years ago and the vagina had undergone the characteristic atrophy subsequently. In a second case the vagina was somewhat shorter than normal due to an old perineal tear that had not been repaired but in the third case, the pelvic organs were absolutely normal and no explanation could be given for this unusual accident.

Polypoid Adenoma of the Uterus.—One of the very frequent forms which tumors of the uterus take is that of polypus and it is not unusual to hear this term used as though it constituted a diagnosis of a condition. It is plain, however, as emphasized by STRONG (*Am. Jour. Obst.*, 1919, lxxix, 502), that the word relates merely to external form and tells nothing of the structure and hence nothing of the nature of a tumor. There are a definite number of pathological conditions which may assume this form and these are generally not especially difficult of recognition in the gross specimen, so that it would be more satisfactory to speak of such tumors according to their specific class using the word "polypus" as a qualifying adjective, thus, "myoma polyposum," etc. What are perhaps most commonly meant when polypi of the uterus are spoken of are adenomata, either of the cervix or corpus uteri. These are tumors of common occurrence, but they have received rather scanty attention in text-books and reports, since their importance clinically has been considered to be slight. During the past five years there have occurred at the Woman's Hospital in New York City several cases where such polypoid adenomata have developed into malignancy of a type which appears to have striking individual characteristics. It should be noted that the polypoid form of these tumors is but a mechanical and secondary effect of the special region in which a tumor is produced and that it has no pathological significance in itself although it frequently does have a clinical significance which may be important, such as hemorrhage and necrosis, both due to interruptions in the blood supply. Pathologically, these tumors may be adenomata, myomata, carcinomata or sarcomata, or they may be an evidence of a simple polypoid hyperplasia of the uterine mucosa. Microscopically, the adenoma has in general all the characteristics that the hyperplasia has not, that is, the glands are irregular in size and outline, their cells show irregularities of arrangement and form and the relationships between gland and stroma are widely disturbed. The basal layer has the adenomatous changes as marked as the rest of the mucosa instead of the relatively simple glands of the normal basalis, According to Strong, there is no difficulty in recognizing an outspoken adenoma but the changes which separate it from simple hyperplasia are all relative and not absolute. The reason that uterine adenomata are polypoid is a physical one, namely, that they are surface tumors and represent non-invasive proliferations of simple glands, and the increase in bulk produced by the proliferation, being non-destructive of other tissue, tends to grow in the direction of least resistance, therefore, on a surface, the proliferation is outward.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
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Determination of the Length of Life of Transfused Blood Corpuscles in Man.—It is of interest and importance to know the relative length of life of red blood cells which have been transferred from one individual to another. Some attempts have been made to estimate this time, by injecting the corpuscles of widely different species into each other; or by transferring the nucleated corpuscles of birds into mammals with non-nucleated cells and observing the time of disappearance. These experiments introduce factors having no bearing upon the problem of homologous transfusion. ASHBY (*Jour. Exper. Med.*, 1919, xxix, 267) made use of the technic for grouping human erythrocytes into four groups. The corpuscles of group I are agglutinated by the serum of all other groups, but its serum has no agglutinating property. The sera of groups II and III agglutinate each other's corpuscles. Serum of group IV agglutinates all other corpuscles but group IV corpuscles are not agglutinated by any serum. It follows then that an individual in group I may receive the blood of any of the groups and that the blood of group IV may be given to any of the groups without danger. An individual having group IV blood may serve as a universal donor. When corpuscles of one group are transferred to any individual of another group, they may be recognized in the circulation by the difference in the agglutinating qualities. This fact was observed in test-tube mixtures of different bloods when it was found that the proportion of agglutinating cells was in relation to quantitative mixture of the two kinds of cells. The author found it possible to apply this to a study of cases after transfusion. After a recipient has been transfused with blood of a group other than his own, specimens of his blood treated with a serum that will agglutinate his own corpuscles, show unagglutinated corpuscles in large numbers. These agglutinated cells are the transfused corpuscles and their count is a quatitative index of the amount transfused. The life of the red cells was estimated at thirty days and over.

Observations on the Wassermann Reaction.—LEWIS and NEWCOMER (*Jour. Exper. Med.*, 1919, xxix, 351) compared the use of the cholesterin antigen with the acetone insoluble antigen of Noguchi. In the experiments the antigens were applied in different tests. The Noguchi antigen was used according to the recently devised test in which use is made of the native human complement without the addition of guinea-pig serum. The cholesterol antigen was used in conjunction with the antisheep hemolytic system. It is, therefore, impossible to fully compare the results regarding the comparative value of the antigens. The results are nevertheless interesting in illustrating identical

results obtained by the two methods and from similar reactions obtained in the majority of the remaining cases. Nevertheless in a certain number of instances a four plus positive cholesterin reaction was obtained along with a negative Noguchi. In other instances exactly the reverse was found. The authors offer no interpretation for the latter result. In a number of cases without evidence of syphilis, but suffering from a variety of febrile diseases, various grades of positive reactions were obtained. The tests are not alone useful for the purpose of diagnosis but also in controlling treatment. The authors conclude "that the Wassermann reaction alone, by whatever method it may be done, can only be used in the diagnosis of syphilis in conjunction with the presumption based on other grounds. That it fails to appear in a considerable number of syphilitics is well known. That the reaction is positive in other conditions is not so generally recognized."

Pathology of Epidemic Influenza.—There has been considerable variation in opinion concerning the important lesions of epidemic influenza and the cause of death. The different interpretations which have been made upon the pathological findings at autopsy have led to a confusing nomenclature which has made it difficult for the clinician to correlate his clinical findings with the pathologist's reports. The terms bronchopneumonia, lobar, lobular, diffuse and interstitial pneumonia have left him "far at sea," and have given him little assistance in the study of subsequent cases. But the difficulties in the study of the pathology of influenza do not alone lie with the varying interpretations by different observers, but it has been amply demonstrated that in different regions the nature and distribution of the lesions varied quite considerably. There are two main factors which have led to the dogmatic deductions so largely at variance with each other: (1) It has been found that the bacterial agents associated with the B. influenzæ differ quite widely in different communities; in some regions the B. influenzæ was prevalent in fairly pure culture; in others it was associated with streptococci, staphylococci, pneumococci, M. catarrhalis or B. Friedländer; grouping of these organisms seemed to have a material influence on the inflammatory process of the respiratory tract, as well as upon the constitutional manifestations. (2) The time of death, whether during the height of the acute epidemic or during the period following appeared to give results that are not entirely comparable. Where reports have been made upon autopsies carried out during the intensity of the epidemic a great similarity in the findings is obtained. Such findings differ, however, from the reports of cases dying late in the disease with their manifold complications. Lyon (*Jour. Am. Med. Assn.*, 1919, lxxii, 924) reports upon 56 autopsies which were performed during the four weeks of the acute epidemic. The average duration of life after the onset was twelve days with the shortest of three days. Cyanosis was common about the head and face. Icterus was observed in six cases. The cases coming to autopsy during the first period of their acute illness showed as the outstanding lesion a hemorrhagic and serous pneumonia. This lesion was most conspicuous in the lower lobes but involved all lobes. There was always some air remaining within the involved tissue. The only reason why the entire five lobes of the lung were not uniformly involved was that death occurred before this was accomplished. Fol-

lowing this type of pneumonia and often present with it was a purulent pneumonia, lobular or patchy in distribution and sometimes even showing lobar characters. The lobar nature of this condition was the result of confluence of a number of lobular patches. The distribution of the lobular process was quite irregular and not confined to any lobe or portion of a lobe. Slight emphysema was not uncommon. Abscesses were not observed in his series. The bronchial lymph nodes were commonly enlarged and edematous. Pleurisy with effusion was common often being blood stained and still more frequently showing hemorrhagic lesions in the pleural walls. Only two cases showed empyema. The heart showed little change other than a mild grade of dilatation on the right side. The lesions of the spleen, liver and kidneys were not severe and usually of the type of granular degeneration. An interesting report to compare with this is that of MacCallum (*Jour. Am. Med. Assn.*, 1919, lxxii, 720) who differs quite frankly in his findings and conclusions. MacCallum reviews some of the bacteriology as observed in three different groups of cases. He is opposed to the consideration of the B. influenzæ as the important agent in our recent epidemic. The causative agent he states is unknown, and it produces great lowering of resistance to bacterial invasion and is often followed by pneumonia caused by different types of pneumococci, staphylococcus aureus, streptococcus hemolyticus or the influenza bacillus. Thus in his consideration the pneumonia is a sequel or complication of influenza and is due to different organisms, depending upon regional distribution. From his findings he attempts to classify pneumonia according to the reactions induced by these different bacteria. Thus he speaks of a pneumococcal pneumonia, staphylococcal pneumonia, streptococcal pneumonia and pneumonia produced by B. influenzæ. The pathological picture which he gives for the pneumococcal pneumonia is not the one which is familiarly known to us as lobar pneumonia and which occurring endemically and epidemically has long been recognized as a distinct pulmonary reaction with definite clinical and pathological characters. In fact his description of pneumococcal pneumonia corresponds more clearly with the pneumonia of epidemic influenza as described by Lyon. The epidemic disease, influenza, is viewed by MacCallum as comparable in many respects to measles and other acute exanthemata and is not necessarily a disease involving the respiratory tracts.

How the United States is Meeting the Tuberculosis War Problem.—Buschnell (*Am. Rev. of Tuberculosis*, 1918, ii, 387) gives an interesting summary of the work of the Government in meeting the problem of the tuberculous soldier. From the very beginning of the mobilization of troops steps were taken to examine all applicants for the earliest signs of tuberculosis. Methods of examination were necessarily different from those of civil life. The statements of the men could not be taken at their face value as some desired to conceal facts, while others, not desiring to enlist, might give a past history of infection when none had existed. Moreover, diagnosis must be upon positive marked signs and symptoms as the need of men was great and the examinations had to be rapid to avoid unnecessary delay and to prevent the entrance of claims for disabilities incurred in line of duty. From the total number of examinations made only 10,000 men were excluded from the National

Guard and the National Army. The majority of these cases were diagnosed within a month or two after entrance into service in which case, if the disease were of a chronic type, it is evident that the disability must be classed as not in line of duty and not entitling the soldier to a pension. As the tuberculous soldier costs the Government on an average of $1000 for pensions, something over $5,000,000 was saved by these exclusions. If the examinations had not been made 10,000 men at an average cost (according to Canada's estimate) of $5000 would have been returned from Europe. For those who are returning and who developed active tuberculosis abroad the Government has provided hospitals in different parts of the United States with a total capacity (September, 1918) of 1305 beds. Physicians experienced in internal medicine and especially in tuberculosis are in great demand, as well as trained lay workers who will serve in teaching the returned soldier how to meet his new life. Because of the treatment prescribed for the tuberculous patient which means months of rest and quiet the problem is a very difficult one. The best results have been gained when the patients are treated far enough from family and friends that frequent visits home are impossible. A stern enforcement of the standardized course of treatment with a tact and kindly sympathy that will inspire the patient with the hope of recovery is expected to accomplish all that is desired in the reconstruction of the tuberculous soldier.

Regulation of the Intestinal Flora of Dogs through Diet.—TORREY (*Jour. Med. Res.*, 1919, xxxix, 415). The author used dogs for these studies because the intestinal flora more closely resembles that of human adults than does that of most other animals. Moreover dogs offer many advantages over rats, cats and monkeys. They eat a variety of food cleanly and quickly; the stools are generally moist, in ample amount and easily obtained; the flora seems more readily modified through diet probably due to the fact that the large intestine in dogs is relatively very short; they are more easily handled and less fastidious. Between four and five hundred fecal specimens were examined from some dozen dogs and the dietary effect determined of various sugars and starches, animal and vegetable proteins and fat on the number and types of bacteria in the intestinal content. Torrey used a number of special media and methods in estimating the variety of bacteria and their relative proportion. Stress is laid on the presence of B. coli, B. acidophilus, streptococcus, B. bifidus, anaërobic spore bearers, H_2S producing bacteria, the degree of putrefaction, gas production and the appearance of direct stained smears. The factors of weight in determining the growth and continuance of bacterial types in the intestinal tract are given as follows: (1) chemical character of the diet particularly the availability of the decomposition products for the metabolism of different bacterial types; (2) the completeness of the digestion and absorption of food within the small intestines; (3) the rapidity and degree to which the food residue is eliminated; (4) symbiosis and antagonism between bacterial groups. With man, factors (2) and (3) are of fundamental importance and dietary changes may not alter unfavorable bacterial conditions if these factors are at fault. Both of these factors act so vigorously in dogs that almost any type of fecal flora may be established by merely changing the diet. In a number of the experiments the animals were sacrificed and the bacterial flora

determined at various levels of the intestinal tract. A purely fermentative flora is simple in type and embraces only a few varieties of bacteria In adults it is dominated by the B. acidophilus, and in breast-fed infants by B. bifidus. In a fermentative flora of a far more common type among adults, B. coli is predominant, A markedly putrefactive flora is complex and contains many varieties of bacteria. Either of two carbohydrates, lactose or dextrin, when added to a meat and rice diet develop a markedly fermentative flora, B. acidophilus dominating and almost completely suppressing the proteolytic types, even including B. coli. A diet of bread (dextrin) and milk (lactose) gave similar results. Saccharose, maltose and glucose gave changes much less marked; the former a moderate change toward a fermentative flora; the two latter little or no alteration. When unboiled milk was given, B. coli and streptococci predominated; while with boiled milk streptococci and B. acidophilus. Starchy foods, white bread, potatoes and beans, all tended to eliminate obligate putrefactive bacteria, rice was less effective. Proteins of mammalian tissue (beef hearts) markedly encouraged the growth and activity of the obligate putrefactive bacteria while a diet of fish did not do so. Milk casein showed far less tendency to give a putrefactive flora than did meat. Vegetable proteins did not offer the slightest encouragement to the growth of intestinal putrefactive types of bacteria. Fat had little or no effect, with large amounts there occurred an apparent reduction within certain groups. This paper is of special importance to all interested in bromatology; the experiments and methods are clearly described; the conclusions are logical and too broad interpretations are avoided.

Perfusion Experiments in the Study of Cellular Anaphylaxis.—Two main theories have been offered regarding the mechanism of anaphylaxis. One group of observers claim that the phenomenon is dependent upon certain substances present in the circulating blood which act upon the antigen and convert it into toxic substances, while other individuals claim that the reaction is dependent upon the cellular activity of particular tissue which became sensitized to the antigen. The adherents to the cellular theory demonstrated the specific avidity of certain tissues after removal of the blood content by perfusion. LARSON and BELL (*Jour. Infect. Dis.*, 1919, xxvi, 185) studied the efficiency of the perfusion method in completely removing the blood from different organs. In carrying out perfusion with Locke's solution they particularly studied the liver and lungs of rabbits, and found that at the end of an hour the effluent still contained some blood and albumin. This was more prominently demonstrated if the experiment was interrupted and then the perfusion renewed. In such instances more albumin and blood appeared in the second effluent. They found, moreover, that if they colored the perfusing fluid with India ink, only particular regions of the liver and lung became stained by this solution. It appeared that in the ordinary perfusion method the easiest route was followed by the perfusing fluid and it did not necessarily travel all of the blood channels. Thus when the experiment was interrupted small quantities of the residual blood again made its appearance in the solution. The authors claim that the perfusion methods used in the experiments for demonstrating the cellular theory of anaphylaxis are insufficient to entirely remove the blood from the organs.

HYGIENE AND PUBLIC HEALTH

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Effective Malaria Control in a Rice-field District.—GEIGER, PURDY and TARBETT (*Jour. Am. Med. Assn.*, March 22, 1919, No. 12, lxxii, pp. 844–847) state that malaria has been eliminated from a typical rice-field district. The question of the flight of Anopheles quadrimaculatus may of necessity be regarded from two angles, that of experiment and that of observation. In one, the largest experiment of its kind ever undertaken in the United States, the record flight was one mile. In the other observation there has been recorded continuously and on different occasions a flight of one and seven-tenths miles. The use of 10 grains of quinin sulphate by the mouth for sterilization of the blood of malaria carriers is evidently efficient for one malaria season if used actively over a period of thirty days. The completely negative clinical history of the nineteen malaria carriers discovered on microscopic examination indicates, on the one hand, an immense difficulty in obtaining complete malaria control, but emphasizes, on the other hand, the importance of the detection of human carriers.

Persistence of the Virus of Poliomyelitis in the Nasopharynx.—FLEXNER and AMOSS (*Jour. Exper. Med.*, April 1, 1919, pp. 379–395) state that the epidemiology of poliomyelitis has still to be worked out in detail, as many factors governing the spread of the disease remain to be discovered. That the virus or microbic cause is communicated by personal contact is now generally admitted. That the virus occurs in the nasopharynx, which constitutes the chief locus of ingress and egress to and from the body, is also conceded. The fact that the virus has been, if rarely, detected in healthy persons who have been in intimate contact with early cases of poliomyelitis, and even in certain individuals who have recovered from the acute effects of the disease, has led to the generalization that like some other diseases of bacterial origin, and notably epidemic meningitis, healthy and chronic carriers of the virus are frequent. This view has received its main support from Kling, Pettersson and Wenstedt, whose studies have been discussed. A critical analysis of the basis of their contention fails, however, to carry conviction, and the doubt which has arisen as to the true interpretation of their results is deepened by the more searching tests of Flexner and Amoss. The results of their experiments conform closely with clinical experience in the United States, at least, and especially with the observations made by epidemiologists in the course of the wide

epidemic in New York State and elsewhere during the summer and autumn of 1916. The conclusion reached at that time was to the effect that the communicability of the disease was a phenomenon chiefly of the early stages, while the frankly paralyzed person and the convalescent were to be feared much less. The authors state that in their experiments infection was secured with tissues obtained during the first week, approximately, of the disease, but not at later periods. The virus of poliomyelitis occurs in the nasopharynx of man and monkeys. In man it has been detected by the inoculation test in washings from acute cases, rarely in similar washings from healthy contacts, in the nasopharyngeal tissues obtained from fatal cases in the first week of infection, but rarely, if ever, from nasopharyngeal tissues removed surgically at later periods in the course of the disease. In monkeys, also, the virus has been detected in the secretions from acute experimental infections, in the nasopharyngeal tissues derived from early cases and rarely from cases several weeks or months after recovery from the acute symptoms. The inoculation of tonsils and adenoids obtained from cases of undoubted poliomyelitis either yielded definite results in the form of typical paralysis and histological lesions in the central nervous organs of the monkeys injected or no symptoms or lesions which could be confounded with poliomyelitis. The indefinite symptoms and atypical lesions described in a certain class of inoculated animals by Kling, Pettersson and Wernstedt were not encountered in the experiments of Flexner and Amoss. The deduction from the experiments reported is to the effect that the virus is regularly present in the nasopharynx in cases of poliomyelitis in the first days of illness, and especially in fatal cases; that it diminishes relatively quickly as the disease progresses, except in rare instances; and that it is unusual for a carrier state to be developed. Hence the period of greatest infectivity of patients would appear to be early in the disease, which is probably the time at which communication of the virus from person to person takes place. Available evidence proves that healthy carriers of the virus occur. The authors, however, possess data which indicate the frequency with which carriage arises. The fact that even after a severe and wide epidemic, such as occurred in the United States in 1916, the disease may virtually disappear within two or three years, points to the probability that enduring carriers of the active virus, whether healthy or chronic, are of exceptional occurrence.

The Role of the Hand in the Distribution of Influenza Virus and the Secondary Invaders.—LYNCH and CUMMING (*Military Surgeon*, December, 1918) state that influenza, as well as the other so-called airborne or respiratory diseases, is essentially a hand-to-mouth infection. There are major and minor modes of transmission by indirect contact: by the former through tepid mess-kit wash-water and by the latter through intermediate objects, the hand being the conveyor in both instances. Among troops approximately 75 per cent. of the cases arise by the major route. This applies to troop transports as well as camps. Transmission by direct contact is only subsidiary to the indirect routes. The adoption of a universal method of washing mess-kits in boiling water will enormously reduce the prevalence of all mouth-borne infections. The prevention of the hand-to-mouth infections may

be accomplished by any measure which will prevent the unclean hand from visiting the mouth and nose and by the thorough cleansing of the hand after all such visits. The incubation period of influenza would appear to be two or three days. An epidemic of influenza among troops may be controlled by elimination of hand-contaminated dish water.

The Effect of Heat, Age and Reaction on the Antiscorbutic Potency of Vegetables.—HESS and UNGER (*Proc. Soc. of Exp. Biol. and Med.*, 1919, No. 4, xvi, p. 52) found that it required 35 gm. of the carrots used to feed laboratory animals to afford protection against scurvy to a guinea-pig. After the carrots had been cooked for three-quarters of an hour their addition to the dietary proved insufficient to protect. This was true even if the water in which they were boiled had been acidulated by the addition of 10 per cent. of vinegar, the only difference noted in the latter test being a less marked loss of weight. A parallel test was carried out with carrots which had been picked only a few days previous to the experiment. It was found that, even subsequent to cooking, 35 gm. of these carrots, when added to the dietary of hay, oats and water, were fully capable of protecting the animals. It is evident, therefore, that in a consideration of vegetables as a foodstuff we must take into account the factor of freshness. In dietetics this difference is intestified by the fact that older vegetables are tougher and therefore require and receive more prolonged cooking, thus further lessening their antiscorbutic value. The water in which the vegetables were cooked possessed little or none of the accessory factor, although 40 c.c. per capita were fed to the guinea-pigs; the animals did not, however, lose weight as rapidly as those receiving tap water. Five c.c. of canned tomatoes are sufficient to protect a guinea-pig from scurvy. If such tomatoes are boiled for five minutes their potency is slightly diminished, so that they should not be subjected to cooking when employed as an antiscorbutic for infants. Their efficacy was not diminished by rendering them slightly alkaline to phenolphthalein. Orange juice which had been made $\frac{n}{20}$ alkaline to NaOH was found to be just as potent as in the acid state. The tomato as well as the orange juice was given by a pipette one-half to three-quarters of an hour following alkalinization. Neither of these antiscorbutics, however, will retain their power long after they have been rendered alkaline. In judging of the effect of alkalinization or of heat it is highly important to consider the length of time to which the antiscorbutic has been subjected to this influence.

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INDEX.

A

Abdominal section, delivery by, 290
Abscess, pulmonary, 724
Adenocarcinoma of intestine, 54
Adenomyoma uteri, 721
Agglutination reaction of meningococcus against carriers, 443
Amyl nitrite in mitral stenosis, 135
Anemia, pernicious, 400
  post-malarial, 430
Anopheles larvæ, 591
Anthrax, human, 782
Antipoliomyelitic horse serum, 432
Antrum, maxillary, irrigating the, 722
Aortic insufficiency, 509
Aortitis, syphilitic, 41
Appreciation of Dr. Richard M. Pearce (June, 1919)
Armstrong, G. E., anatomical changes and histogenesis in gastritis granulomatosa fibroplastica, 35
Arsphenamin, cause of death from, 433
Arthritis deformans and spondylitis in Egypt, 728
  and infection, 567
  protein therapy in treatment of, 125
Asthma, bronchial, treatment of, 717
Ayer, J. B., obtaining cerebrospinal fluid by puncture from cisterna magna, 789

B

Bacillus hystolyticus, biochemistry of, 444
  influenzæ in sinusitis and meningitis, 431
  in throats and saliva, 725
  "Reading," 727
Bacteria, acid production by, 299
  action of freezing temperatures on, 152
Bacteriemias in the agonal period, 298
Bacterium abortus and related bacteria, 307
Bailey, C. V., renal diabetes, 221
Barron, M., mustard-gas inhalation, 808
Bastedo, W. A., treatment of dangerous hematemesis, 99
Benedict, A. L., speculations regarding the nature of cancer, 742
Benzine poisoning, frequency of, 450
Berger, Emil, binocular loupe for examination of functional troubles of the pupil, 208
Bichloride of mercury poisoning, 348
Binocular loupe for examination of functional troubles of the pupil, 208
Biochemistry of Bacillus hystolyticus, 444
Blake, Clarence John, obituary of (April, 1919)
Blankets and uniforms, sterilization of, 448
Blindness, temporary, 441
Blood, collecting of, for Wassermann test, 442
  corpuscles in man, 859
  creatinine of, in nephritis, 674
  cysts of the orbit, 441
  meningococcus in, 155, 299
  transfusion, 151, 580
Bone, buried, study of, 847
Botulism, 134, 451
Bovine mastitis, 448
Boyer, E. E. H., carcinoma of vermiform appendix, 775
Brain, changes of, in paresis, 271
Brom cresyl purple and litmus as indicators of tubercle bacilli, 446
Bronchial asthmatics, treatment of, with pollens, 409
Brown, G. E., syphilitic aortitis and its early recognition, 41
Bulimia, case of, 356
Burns and scalds, magnesium sulphate for, 434

C

Camus, reëducation of the maimed, 839
Cancer, 588, 742
  delay in treatment of, 34
  immunity, lymphocytes in, 301
  of internal organs, 444
  in Norway, 720
  occupational, 444
  radium in, 855
  of the stomach, 1
Cancerous diseases in Norway, 149
Cantharis, physiological action of, 717
Carbon dioxide, safe limit of, 447
  in working atmosphere, 447
Carcinoma of the duodenum, 182
  experimental, of animals, 300
  of gall-bladder, 67
  of stomach, 848
  of vermiform appendix, 775
  in a young woman, 722
Cardiothoracic ratio, 513
Cash, S. L., left apical impairment in mitral stenosis, 652

Cerebellar injuries due to gunshot injuries, 127
Cerebrospinal fever, 591
fluid obtained from cisterna magna, 789
meningitis, 568
Cesarean section, 575, 580
scar, rupture of uterus through, 289
Childbirth, painless, 582
Chorio-epithelioma, operative treatment of, 576
Christian, H. A., digitalis therapy, 593
Christian, T. B., pathological changes of the brain in paresis, 271
Circulation, tests of functional capacity of, 634
Clark, E., influenza-pneumonia cases showing gas in fascial tissues, 219
Coff, organs of internal secretion, 843
Colon, sigmoid, contractures of, 435
Color blindness, 303
Congenital dextrocardia, 483
Conjunctivitis, tuberculous, treated with tuberculin, 198
Covey, G. W., mustard-gas inhalation, 808
Crowdy, C. T., adenocarcinoma of intestine, 54
Curettage, removal of intestines during, 585
Cystocele, operation for, 144, 145
treatment of, 146

D

Dana, H. W., heart muscle equations, 750
Danzer, C. S., cardiothoracic ratio, 513
Death, a new sign of, 442
Deaver, J. B., pathological possibilities of neglected gall-stone disease, 733
Dermatitis coccidiosa, 589
Dextrocardia, congenital, 483
Diabetes, renal, 221
Diagnostic and clinical relations of certain tuberculids, 313
Dichlorethylsulphide poisoning, 432
Digitalis therapy, 593
Dinitrophenol, jaundice due to, 154
Diphtheria and diphtheroid organisms in open wounds, 147
Diseases, toll of the degenerative, 730
Dock, G., bulimia, with remarks on the causal treatment of some functional diseases, 356
Dogs, intestinal flora of, regulated through diet, 862
Drugs and poisons, absorption of, through the vagina, 143
Dunham, J. D., epidemic of typhoid fever at Hot Springs, N. C., 608
Duodenal ulcer, 74
Duodenum, carcinoma of, 182

E

Eclampsia, blood in, 141
Ectopic pregnancy, 586
Emphysema, acute pulmonary, 170
Empyema, 156, 571, 572
Encephalitis lethargica, 443
Epiglottectomy by transthyrohyoid access, 723
Epinephrin for the morphin habit, 573
Epiphyseal cartilage plate, injury to, 846
Epithelioma of the scalp, 590
Esophagus, stricture of, 725
Essick, C. R., obtaining cerebrospinal fluid by puncture of cisterna magna, 789
Ethmoiditis in young subjects, 441
Exercise, effect of, on undernourished men, 130

F

Farr, C. E., delay in treatment of cancer, 34
Fats, function of, in immune processes, 731
Femur, treatment of fracture of, 847
Fever, trench, 154
Fractures, compound, 571
Frick, D. J., treatment of soldiers infected with hookworm at Camp Beauregard, La., 189
Friedenwald, J., perforation in cancer of the stomach, 1
Fundus, observation of, during temporary blindness, 441

G

Galactagogue, 573
placental tissue as a, 853
Gall-bladder, carcinoma of, 67
disease complicating pregnancy, 143
Gall-stone disease, 733
Gas, mustard, poisoning 432
Gastric ulcer, 74
Gaucher's disease, 366
Gibbon, J. H., advancement in treatment of wounds and infections resulting from the war, 764
Glycosuria, study of an unusual, 201
Goitre among draft men, 567
Goodman, E. H., diagnosis of mitral stenosis, 112
Goodman, E. H., differential diagnosis between mitral stenosis and aortic insufficiency, 509
Goodman, E. H., Graham-Steell murmur in mitral stenosis, 206
Goodman, E. H., left apical impairment in mitral stenosis, 652
Graham-Steell murmur in mitral stenosis, 206
Grosh, L. C., acute pulmonary emphysema, 170

Gross, M. H., modern aspect of treatment of ulcus ventriculi, 8
Guinea-pigs, scurvy in, 452
Gunshot affections of large joints, 845
fractures, ununited, 845
injuries, 127
Gynecology, radium in, 296

H

Hall, C. C., roentgen-ray intoxication, 453
Hamley, W. H., epidemic cerebrospinal meningitis at Camp Beauregard, La., 210
Harris, W. H., a mesothelioma of both suprarenal bodies and both lungs, with hemothorax, 602
Head, G. D., primary carcinoma of the third portion of the duodenum, 182
Head, rotation of, by forceps, 853
Headaches, pituitary, 716
Heart disease, prognosis in, 5
muscle equations, 750
Heat, age and reaction on antiscorbutic potency of vegetables, 866
Held, I. W., modern aspect of treatment of ulcus ventriculi, 8
Hematemesis, 99
Hemorrhages in parturient women, 580
tubal and ovarian, 584
Homans, J., pain in gastric and duodenal ulcer, 74
Hookworm, treatment of soldiers infected with, 189
Hopkins, A. H., climacteric hypertension, 826
Horse serum, 432
antipoliomyelitic, 432
Horses, pneumococcus infection of, 726
Hour-glass stomach, 570
Human anthrax, 782
Hunger by drugs, control of, 288
Hypertension, climacteric, 826
Hysterectomy, effect of, upon the ovarian function, 579
ovarian function after, 584

I

Infection, droplet, and its prevention by the face mask, 737
Infections, treatment of, resulting from the war, 764
Influenza in children, 770
epidemic, 860
in newly born infant, 852
pandemic of, 308
pneumonia cases showing gas in fascial tissues, 219
Spanish, 432
treatment of, 849
virus, distribution of, 865
Intestine, adenocarcinoma of, 54
protozoal infections of the, 492
Intoxication, roentgen-ray, 453
Intravenous injections, 573
Irritable heart, fatigue in, 850
of soldiers, epinephrin in, 287

J

Jaundice, chronic, 500
Johnston, J. I., chronic jaundice, 500

K

Kahn, M. H., tests of functional capacity of the circulation, 634
Keratodermia, symmetrical, 589
Killian, J. A., prognostic value of the creatinine of blood in nephritis, 674

L

La Fétra, L. E., influenza in children, 770
Labor, injuries of, 139
injury, recognition and management of, 581
Landry, A. A., cerebrospinal meningitis at Camp Beauregard, La., 210
Langstroth, L., study of an unusual glycosuria, 201
Larynx, angioma of, in a child, 724
papillomata of, 724
Lead poisoning, frequency of, 450
turpentine and benzin poisoning, 136, 450
Lesions of sacro-iliac joint, 570
Lewisohn, R., clinical results in transfusion of citrated blood, 253
Lichen planus treated by lumbar puncture, 590
Lime and halazone in disinfection of drinking water, 732
Lobar pneumonia, 300
Lumbar puncture, 83

M

McGlannan, A., perforation in cancer of the stomach, 1
MacCarty, W. C., a biological conception of neoplasia, 657
Magnesium sulphate, application of, to scalds and burns, 434
in treatment of spastic contractures of rectum and sigmoid colon, 435
Malarial control in rice-field district, 864
Mandlebaum, F. S., Gaucher's disease in adults, 366
Mask, face, 732
Mastitis, bovine, 448
Mellon, R. R., trichomyces infections in Western New York, 540
Meningitis, 431
basilar, 58
cerebrospinal, 568

Meningitis, control of treatment of, 306
epidemic, 306
Meningococcus carriers, 148
reaction of, against carriers, 443
Menopause, vertigo of, 438
Menorrhagia, radium treatment of, 719
Mercury, poisoning by bichloride of, 348
Mesothelioma of suprarenal bodies of both lungs, 602
Metastases, multiple skin, 444
Metritis, pathology of chronic, 439
Migraine, a study of, 361
Mitchell, J. W., diabetes mellitus with syphilis, 700
Mitral stenosis, 112, 509, 652
Morphin habit, 573
Mucor infection, 445
Multiple endothelioma of the skin, 236
Mustard gas poisoning, 432
inhalation, 808
Myers, V. C., value of the creatinine of the blood in nephritis, 674
Myoma uteri, 856

N

Nares, bony occlusion of, 723
Neoplasia, a biological conception of, 657
Nephritis, 674
trench, 126
Nerves, peripheral, 569
Neurokeratin stain, 729
Neuroplasty, 569
Norris, G. W., medical impressions of the war, 628
Nosebleed complicating pregnancy, 138
Nuzum's antipoliomyelitic serum, 312

O

Obituary of Clarence John Blake (April, 1919)
Obstetrical operations, 291
Ocular affections in typhoid, 440
diseases, tuberculin in, 442
Oculogyration, 695
Oertel, H., anatomical changes and histogenesis in gastritis granulomatosa fibroplastica, 35
Ophthalmoplegia, bilateral, 695
Orbit, blood cysts of, 44
sarcoma of, 723
Ozone in swimming-pool disinfection, 452

P

Paralysis agitans, 431
Parathyroidectomy, 149
Paresis, 271
Parotitis, experimental, 309
Paterson, R. C., granular tuberculous conjunctivitis treated by installations of tuberculin, 198
Pearce, Richard M., appreciation of (June, 1919)
Pediculosis pubis due to head louse, 589
Perfusion experiments in anaphylaxis, 863
Peritonitis, 797
Pernicious anemia, 400
Pickard, R. J., protozoal infections of the intestines, 492
Pituitary headaches, 716
Pituitrin, dangers of, 140
Placenta previa, 580
treatment of retention of, 140
Placental tissue as a galactagogue, 575, 853
Pneumonia, 446
experimental chemical, 298
organizing, 446
Poisoning by bichloride of mercury, 348
by mustard gas, 432
Poliomyelitis, attempts to induce, 449
epidemic, 312
in small animals, 449
studies of, 449
transmission of, 304
virus of epidemic, 303
Pollens, treatment of asthmatics with, 409
Pollock, R., protozoal infections of the intestines, 492
Pools, swimming, 591
Post-malarial anemia, 430
Pregnancy, ectopic, 586
extra-uterine, 141
gall-bladder disease, 143
status epilepticus in, 138
toxemia of, 579
Pregnant women, influenza occurring in, 851
Première séance consagree à la biologie de guerre, 132
Prolapse in the aged, 855
Prostate, hypertrophied, 848
Prostatic obstruction, 390
Protein therapy in arthritis, 125
Protozoal infections of the intestines, 492
Psychiatric material in naval prison, 311
Puerperal septic uteropelvic thrombophlebitis, 137
Pulmonary circulation, 548
Purgation, 436
of patients before operation, 436
pre-operative treatment of, 436

Q

Quinby, W. C., standardization of methods in cases of prostatic obstruction, 390

R

Rabinowitz, M. A., hematogenous streptococcic peritonitis, 797
Radium in gynecology, 296
therapy in uterine cancer, 294
in treatment of cancer, 295
Rat and poliomyelitis, 308
Rectovaginal lacerations, repair of, 144

Rectum, contractures of, 435
Regan, C., human anthrax, 782
Regan, J. C., human anthrax, 782
Regan, J. C., lumbar puncture, 83
Renal diabetes, 221
  pain, 720
Respiratory disease among troops, 297
Reviews—
  Abstracts of War Surgery, 712
  Adler, Histopathological Technic, 559
  Allen, Local and Regional Anesthesia, 713
  American Urological Association, 123
  Bacon, Otology, 119
  Bland-Sutton, Tumors, 561
  Brown, Oral Diseases and Malformations, 705
  Collected Papers of Mayo Clinic, 711
  Craig, Wassermann Test, 124
  Davis, Dispensaries, 558
  De Lee, Obstetrics, 564
  Duval, War Wounds of Lungs, 280
  Ewing, Neoplastic Diseases, 563
  Fisher, Effect of Diet on Endurance, 712
  Foote, Materia Medica and Therapeutics, 282
  Frazier, Surgery of Spine and Spinal Cord, 837
  Graves, Gynecology, 122
  Gray, Anatomy, 704
  Handerson, Gilbertus Anglicus Medicine of the Thirteenth Century, 841
  Hess, Infant Feeding, 121
  Hirst, Gynecology, 559
  Howe, Humane Society of Massachusetts, 840
  Huggins, Amputation Stumps, 282
  Hughes and Banks, War Surgery, 841
  International Medical Annual, 284
  Jones and Fisher, Equilibrium and Vertigo, 565
  Joslin, Diabetic Manual, 555
  Koplik, Diseases of Infancy and Childhood, 706
  Lamb, Nose and Throat, 120
  Leftwich, Therapeutics, 284
  Loeb, Movements, Tropisms and Animal Conduct, 428
  Mackenzie, Action of Muscles, 842
  Mackenzie, Symptoms and Their Interpretation, 562
  Mallory and Wright, 561
  Manual of Splints and Appliances for the Medical Department of the United States Army, 281
  May, Venereal Diseases, 286
  Mayer, Gunshot Injuries, 555
  Medical Clinics of North America, 282
Reviews—
  Morison, Bipp Treatment of War Wounds, 276
  Morton, Genito-urinary Diseases, 285
  Oxford Loose-leaf Surgery, 556
  Price, Diseases of the Heart, 558
  Radasch, Histology, 119
  Report of Department of Pathology of Johns Hopkins University, 844
  Ringer, Clinical Medicine for Nurses, 714
  Satterthwaite, Diseases of Heart and Bloodvessels, 838
  School Children of England, 707
  Shera, Vaccines and Sera in Military and Civilian Practice, 560
  Sherman, Food and Nutrition, 121
  Sluder, Headaches and Eye Disorders, 120
  Smith, Nose and Ear, 562
  Smithies, Quarterly Medical Clinics, 840
  Surgical Clinics of Chicago, 281
  Tarnowsky, Military Surgery of the War of the Advance, 276
  Todd, Mammalian Dentition, 844
  Trench Fever, 277
  Walter, Human Skeleton, 429
  Warbasse, Surgical Treatment, 427
  Williams, Proteomorphic Theory and the New Medicine, 283
  Witthaus and Scott, Chemistry, 557
  Wittich, Information for the Tuberculous, 713
Roentgen-ray intoxication, 453
  in treatment of cancer, 295
Rosenbloom, J., acute bichloride of mercury poisoning, 348
Rupert, M. P. S., migraine, 361

S

Scabies in military and civil life, 153
Scalds and burns, magnesium sulphate for, 434
Scurvy, 310
  in guinea-pigs, 452
Serum, antitrypsin of, 152
  complement power of, 310
  horse, 432
Shawan, H. K., blood grouping applied to skin grafting, 503
Shick tests for immunity, 731
Sigmoid colon and rectum, treatment of contractures of, 435
Siliceous dust, physiological effects on miners, 302
Simonds, J. P., factor of safety in the pulmonary circulation, 548
Sinusitis, 431
Skin grafting, 503

Skin metastases from cancer of internal organs, 444
Smithies, F., carcinoma of the gall-bladder, 67
Spanish influenza, 432
Spiller, W. G., importance of the motion field in comparison with the form field in failing vision, 483
Spiller, W. G., remarks on oculogyration, 695
Spirillosis, 302
Spirocheta hebdomadis, 309
Sputum, bacilli isolated from, 451
virulence of tubercle bacilli isolated from, 451
Stain, neurokeratin, 729
Sterility, operation for, 721
Sterilization of blankets and uniforms, 448
Stokes, J. H., clinical studies in cutaneous aspects of tuberculosis, 157, 313, 522
Stomach, cancer of, 1
hour-glass, 570
Streptococci recovered from soldiers in France, 727
Streptothrix infection of cows' udders, 307
Swimming-pool disinfection, 452, 591
Synnott, M. J., influenza-pneumonia showing gas in fascial tissues, 219
Syphilis and tuberculosis, 154
pathology of, 153

T

Thrombophlebitis, 137
Thyroid therapy, 125
Tonsils, primary tuberculosis of, 724
Torrey, R. G., acute pulmonary emphysema, 170
Toxemia of pregnancy, 579
Transfusion of citrated blood, 253
Trench fever, 154
nephritis, 126
Trichinosis, serum therapy in, 287
Trichomyces infections, 540
Trinitrotoluene poisoning, 716
Tubercle bacilli isolated from sputum, virulence of, 451
Tuberculids, diagnostic and clinical relations of, 313
Tuberculin in ocular disease, 442
Tuberculosis, 588
and syphilis, 154
Tuboövarian suppuration, 586
Tumors, malignant, in man, 150
Turpentine poisoning, frequency of, 450
Twins, joined, 140
Typhoid bacilli injected into rabbits, 726
in sour milk, 156
Typhoid fever, 608
ocular affections in, 440

U

Ulcus ventriculi, 8
Uniforms and blankets, sterilization of, 448
Uranium poisoning, 445
Urine, specific gravity of, 715
Uterus, adenoma of, 858
double, with torsion of one cornu, 139
mesodermal mixed tumors of, 718
tumors of, treated with radium, 295

V

Vaccination, antimeningitis, 309
Vaccine, Leary's, prophylactic value of, 287
Vaccines, sensitized, in treatment of infections, 293
Vagina, lacerations of, from coitus, 857
Varicella, protective, 310
Vermiform appendix, carcinoma of, 775
Vertigo of the menopause, 438
Virus of poliomyelitis in nasopharynx, 864
Vision, failing, 483

W

Walker, I. C., sensitization and treatment of bronchial asthmatics with pollens, 409
War, medical impressions of, 628
problem in United States, 861
Wassermann reaction, 859
in tuberculous affections of the skin, 588
test, 442
Water at filtration plants, examination of, 306
Wegeforth, P., obtaining cerebrospinal fluid from cisterna magna, 789
Whipple, G. H., roentgen-ray intoxication, 453
White, P. D., prognosis in heart disease, 5
Willius, F. A., congenital dextrocardia, 485
Wilson, E. E., a study of migraine, 361
Wise, F., multiple endothelioma of the skin, 236
Woltmann, H. W., nervous symptoms in pernicious anemia, 400
Wounds, treatment of, resulting from the war, 764

Z

Zingher, A., ventricular puncture for treatment of basilar meningitis, 58

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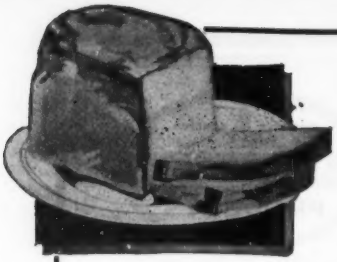

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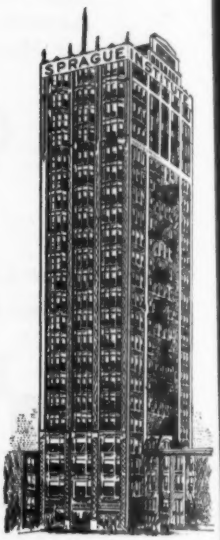

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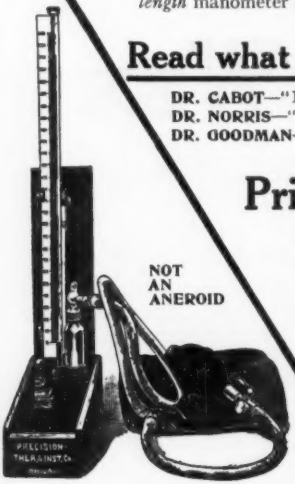

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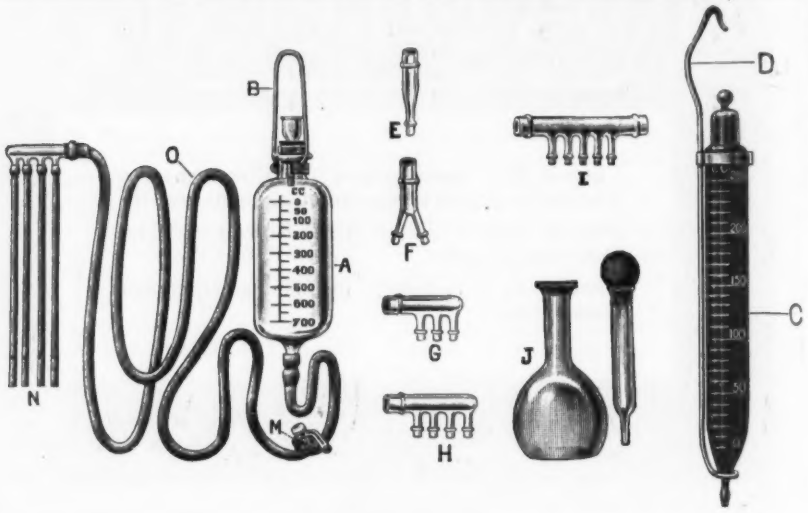

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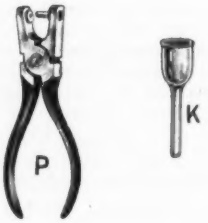

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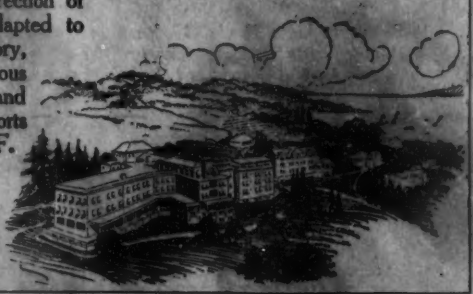

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